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**UNDER THE PATENT COOPERATION TREATY (PCT)  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: Agouron Pharmaceuticals, Inc., et al.

International Appl. No.: PCT/US99/18790

Atty. Docket: 0121-0002PCT

International Filing Date:  
20-August-1999

For: Non-Peptide GnRH Agents, Method and  
Intermediates for Their Preparation

**RESPONSE TO INVITATION TO CORRECT DEFECTS  
IN THE INTERNATIONAL APPLICATION**

Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231

Attention: RO/US

Sir:

In response to the Invitation to Correct Defects mailed on 18-February-2000,

Applicants submit the following:

1. An original, executed PCT Power of Attorney for Haitao Li and James Faust;
2. An original, executed PCT Power of Attorney for David Robert Luthin, Lance Christopher Christie, Yufeng Hong, and Eileen Valenzuela Tompkins;
3. An original, executed PCT Power of Attorney for Mark Brian Anderson, Haresh N. Vazir, Ved P. Pathak, and Genevieve DeGuzman Paderes;
4. Legal documentation demonstrating Gary Friedman's authorization to sign the previously filed PCT General Power of Attorney on behalf of Agouron Pharmaceuticals, Inc.;
5. Substitute sheets 1-440 and 15 sheets of formal drawings. As requested in the Invitation to Correct Defects in the International Application, please note

that the drawings have been moved out of the specification and rendered as separate formal figures. The separate table of compounds have been integrated into the description and page numbered accordingly, as requested. All of the substitute sheets are originals and contain neither overwriting nor copy machine marks. Also, all substitute sheets have had the margins formatted to fit within PCT parameters, as requested; and

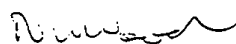
6. A check in the amount of \$50 (fee for 5 extra pages due to making the drawings separate and formal).

Please note that a Request for Extension of Time was filed with the U.S. Receiving Office on 03-March-2000 extending the deadline for responding to this Invitation from 18-March-2000 to 18-April-2000. A copy of the Request and date-stamped postcard is also enclosed.

If the Filing Fee is found to be insufficient for any reason, please charge such deficiency to our Deposit Account No. 50-0622.

Respectfully submitted,

SHANKS & HERBERT



David W. Woodward  
Reg. No.: 35,020

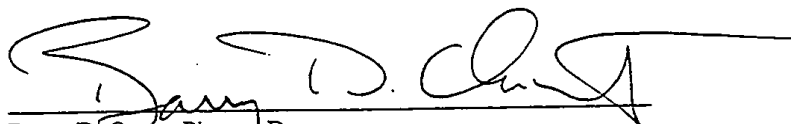
Date: 31-March-2000

TransPotomac Plaza  
1033 N. Fairfax Street  
Suite 306  
Alexandria, VA 22314  
(703) 683-3600

## CERTIFICATION OF CORPORATE SIGNATORY AUTHORITY

I hereby certify that I am an officer of Agouron Pharmaceuticals, Inc. ("Agouron" or the "Company"), a corporation duly organized and existing under the laws of the State of California, United States of America, with signatory authority to sign legal documents on behalf of Agouron. I further certify that Gary E. Friedman, an officer of Agouron having the title of Corporate Vice President, Secretary and General Counsel, also has signatory authority to sign legal documents on behalf of Agouron.

IT WITNESS WHEREOF, I have hereunto set my name and affixed the seal of the Company this 22<sup>th</sup> day of March, 2000.

A handwritten signature in black ink, appearing to read "Barry D. Quart", written over a horizontal line.

Barry D. Quart, Pharm.D.  
President, Research and Development  
Agouron Pharmaceuticals, Inc.

PCT

GENERAL POWER OF ATTORNEY

(for several international application filed under the Patent Cooperation Treaty)

(PCT Rule 90.5)

The undersigned person(s):

(Family name followed by given name; for a full legal entity, full official designation. The address must include postal code and name of country.)

7699 L  
Li, Haitao, 9099 Palmilla Drive #3112, San Diego, California 92122, United States of America

FAUST, James, 15684 Bernardo Center Drive #2010, San Diego, California 92127, United States of America

Hereby appoint(s) the following person as:



agent



common representative

Name and Address

(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

HERBERT, Toni-Junell and WOODWARD, David W.: Both of SHANKS & HERBERT, TransPotomac Plaza,

1033 North Fairfax Street, Suite 306, Alexandria, Virginia 22314, United States of America; and

EVANS, Linda S., Agouron Pharmaceuticals, Inc., Legal Department, 10350 North Torrey Pines Road, La Jolla, California 92037-1020, United States of America

To represent the undersigned before



all the competent International Authorities



the International Searching Authority only



the International Preliminary Examining Authority only

in connection with any and international application filed by the undersigned with the following Office

US

as receiving Office

and to make or receive payments on behalf of the undersigned.

Signature(s) (where there are several persons, each of them must sign; next to each signature, indicate the name of the person signing and the capacity in which the person signs, if such capacity is not obvious from reading this power):

Haitao Li 8/30/99  
Haitao Li

James FAUST 25 Aug. 99  
James FAUST

Date: \_\_\_\_\_

PCT

GENERAL POWER OF ATTORNEY

(for several international application filed under the Patent Cooperation Treaty)

(PCT Rule 90.5)

The undersigned person(s):

(Family name followed by given name; for a full legal entity, full official designation. The address must include postal code and name of country.)

ANDERSON, Mark Brian, 3967 Nobel Drive #260, San Diego, California, United States of America

VAZIR, Haresh N., 10528 Caminito Pollo, San Diego, California 92126, United States of America

PATHAK, Ved P., 4140-157 Via Candidiz, San Diego, California 92130, United States of America

PADERES, Genevieve DeGuzman, 5183 Sea Mist Court, San Diego, California 92121, United States of America

Hereby appoint(s) the following person as:

☒ agent ☐ common representative

Name and Address

(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

HERBERT, Toni-Junell and WOODWARD, David W.; Both of SHANKS & HERBERT, TransPotomac Plaza,  
1033 North Fairfax Street, Suite 306, Alexandria, Virginia 22314, United States of America; and

EVANS, Linda S., Agouron Pharmaceuticals, Inc., Legal Department, 10350 North Torrey Pines Road, La Jolla,  
California 92037-1020, United States of America

To represent the undersigned before

- ☒ all the competent International Authorities  
☐ the International Searching Authority only  
☐ the International Preliminary Examining Authority only

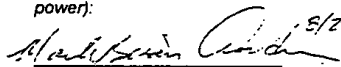
in connection with any and international application filed by the undersigned with the following Office

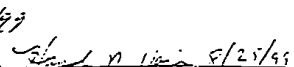
US

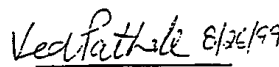
as receiving Office

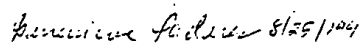
and to make or receive payments on behalf of the undersigned.

Signature(s) (where there are several persons, each of them must sign; next to each signature, indicate the name of the person signing and the capacity in which the person signs, if such capacity is not obvious from reading this power):

 5/25/99  
Mark Brian ANDERSON

 5/25/99  
Haresh N. VAZIR

 5/26/99  
Ved P. PATHAK

 5/25/1999  
Genevieve DeGuzman PADERES

Date: \_\_\_\_\_

PCT

GENERAL POWER OF ATTORNEY

(for several international application filed under the Patent Cooperation Treaty)

(PCT Rule 90.5)

The undersigned person(s):

(Family name followed by given name; for a full legal entity, full official designation. The address must include postal code and name of country.)

LUTHIN, David Robert, 1772 Shadow Mountain Drive, Encinitas, California 92024, United States of America  
CHRISTIE, Lance Christopher, 518 Mynah Place, Vista, California 92083, United States of America  
HONG, Yufeng, 11980 Ashley Place, San Diego, California 92128, United States of America  
TOMPKINS, Eileen Valenzuela, 10129 West Lilac Road, Escondido, California 92026, United States of America

Hereby appoint(s) the following person as: ☒ agent ☐ common representative

Name and Address

(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

HERBERT, Toni-Junell and WOODWARD, David W.; Both of SHANKS & HERBERT, TransPotomac Plaza,  
1033 North Fairfax Street, Suite 306, Alexandria, Virginia 22314, United States of America; and  
EVANS, Linda S., Agouron Pharmaceuticals, Inc., Legal Department, 10350 North Torrey Pines Road, La Jolla,  
California 92037-1020, United States of America

To represent the undersigned before ☒ all the competent International Authorities  
☐ the International Searching Authority only  
☐ the International Preliminary Examining Authority only

in connection with any and international application filed by the undersigned with the following Office  
US as receiving Office  
and to make or receive payments on behalf of the undersigned.

Signature(s) (where there are several persons, each of them must sign; next to each signature, indicate the name of the person signing and the capacity in which the person signs, if such capacity is not obvious from reading this power):

David Robert LUTHIN 8/26/99  
Lance Christopher CHRISTIE 8/25/99  
Yufeng HONG 8/25/99  
Eileen Valenzuela TOMPKINS 8/25/99

Date: \_\_\_\_\_

**UNDER THE PATENT COOPERATION TREATY (PCT)  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Agouron Pharmaceuticals, Inc., et al.

International Appl. No.: PCT/US99/18790

Atty. Docket: 0121-0002PCT

International Filing Date:  
20-August-1999

For: Non-Peptide GnRH Agents, Methods and  
Intermediates For Their Preparation

**LETTER TO PROTEST AND REQUEST FOR ENTRY  
OF SUBSTITUTE PAGES FOR REPUBLICATION**

ATTN: Examiner Nguyen Ngoc-Ho  
Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231

Sir:

This is a Letter of Protest in response to the refusal to accept substitute pages mailed on 25-May-2000 for the above-identified PCT application. We respectfully draw the Examiner's attention to the troubled history of this PCT case, as outlined below.

This PCT application was filed on 20-August-1999. Shortly thereafter, we received the return postcard from the U.S. PCT Branch assigning the application International Application No. PCT/US99/18790. When no further communication was received by November, we began contacting the PCT Help Desk for the status of this case. Several messages were left and went unanswered, which led the undersigned to believe that there may be a problem with this case. The following is an outline of our communications with the U.S. PCT Branch after receiving no response to our status inquiry messages.

I. December 15, 1999. No communication had been received since the 20 August 1999 filing of the PCT application. Status inquiry messages were not being answered. A call was made to the PCT Help Desk line and a message was left requesting status information on this application.



II. December 30, 1999. A call was made to the PCT Help Desk line and a message was left requesting a response to prior queries regarding the status of this application. It was also noted in the message that the Search Report was late.

III. January 3, 2000. There was still no response to our telephone messages. As a result, a written Status Inquiry was filed. To date, a reply was never received from the U.S. PCT Branch to this inquiry.

IV. January 19, 2000. Another call was made to the PCT Help Desk line and a message was left demanding answers. A Mr. Smoot, who left a message for the undersigned, finally returned this call the following day.

V. January 20, 2000. Mr. Smoot's call is returned. Surprisingly, despite the details being left in numerous messages, Mr. Smoot appears to have absolutely NO information on the case, and states that he requires time to research the matter and call us back in a few days.

VI. January 28, 2000. The undersigned confirms that Mr. Smoot had not contacted him again, directly. At this point, the PCT Help Desk line is contacted yet again, and another message left requesting that either Mr. Smoot or anyone contact us immediately with information regarding this case. No response is received.

VII. February 4, 2000. The undersigned confirms that neither Mr. Smoot nor anyone from the U.S. PCT Branch has spoken directly to him since our last message. Yet another message was left at the PCT Help desk line requesting assistance. A second written Status Inquiry was filed. To this date, NO responses have ever been forthcoming on any of the written Status Inquiries.

VIII. February 14, 2000. Eunice answered our call to the PCT Help Desk. We were informed that the application was being held up in the Legal Department in order to ascertain if the invention could indeed be patented. We asked when it would be assigned to an Examiner. Due to the delays, we had not received an Invitation to Correct Defects and Search Report. We also brought to her attention that the Chapter II Demand was due to be filed on March 20, 2000. She stated that there was no timeframe on assignment to an Examiner and there was "nothing anyone can do in these cases, but wait for the Legal Department to make the call."

This same day we contacted Richard Lazarus at the U.S. PCT Branch and explained the situation. He said he would need to research the matter and get back to us.

IX. February 15, 2000. We received a message from Richard Lazarus stating that he was unable to locate the application anywhere and advising us to submit copies of the papers as originally filed. A transmittal letter outlining the problem and requesting that the application be expedited to an Examiner, was submitted to the U.S. PCT Branch with copies of all originally filed documents and the date-stamped postcards. A copy of everything was also sent to WIPO. A response was subsequently received from WIPO acknowledging receipt of said documents.

X. February 25, 2000. We contacted the U.S. PCT Branch to find out if they had expedited the case. Veronica Scales answered the call. She stated that she did not understand what Richard Lazarus was talking about. She further stated that the case is there, and has been all along, as well as being in their central computer. We were told that she would need to investigate and get back with us.

In response to this latest information and the upcoming deadlines, a call was made to the PCT Supervisor, Carol Bidwell. A message was left for Ms. Bidwell that afternoon. However this same afternoon, we received the Invitation to Correct Defects, issued by Georgette Hill, which had been mailed on 18-February-2000. Ms. Bidwell was informed of such when she returned the call.

The Invitation to Correct Defects, requested substantial changes in the international application, i.e., renumbering of pages, reformatting of margins around tables, removing figures from the specification to become separate drawings, etc.

XI. February 28, 2000. We spoke with Carol Bidwell in regard to moving the drawings out of the description and having them rendered formal in response to the Invitation to Correct Defects. She advised that this mostly depended upon how we want the application to look when it published. However, she stated that she would "strongly advise" us to comply with the demands of the Invitation to Correct and that "it would be in your best interest to move the drawings and have them rendered formal." Preparations were then initiated to move the drawings out of the description and render them formal with a draftsman.

XII. March 3, 2000. Realizing the amount of time involved in preparing formal drawings (particularly due to the length of the application), a Request for Extension of Time to Respond to the Invitation was filed.

XIII. March 20, 2000. The Chapter II Demand was filed. At this point we are still trying to fulfill all of the requests made under the Invitation to Correct Defects.

XIV. March 31, 2000. With all of the requests of the Invitation to Correct Defects fulfilled, documents were submitted to the U.S. Patent Office.

XV. April 25, 2000. We received a copy of the published application, which did not contain any of the changes submitted in response to the Invitation to Correct Defects.

XVI. April 30, 2000. We received a communication from the U.S. PCT Branch refusing our Request for an Extension of Time to Respond to the Invitation to Correct Defects. This is nearly two months after the request was filed.

XVII. May 1, 2000. We contacted the U.S. PCT Branch and spoke with Sonya Barnes to explain the troubled history of the case and what were our options. She requested that we allow her time to locate the file and she would call us back. Ms. Barnes returned the call that afternoon. She stated that the Extension of Time was denied automatically due to how far along the case was - the history was not taken into consideration. She stated that she was not yet in receipt of the corrections made in our Response filed on March 31, 2000. She requested that we call back on Friday, May 5, 2000. She would enter and forward the corrections to the International Bureau. She also advised that it would be a good idea to fax the International Bureau at that point and inform them that the changes were coming and request that they republish the application.

XVIII. May 2, 2000. A call was made to David Barnes of the World Intellectual Property Organization (WIPO). He was given the history of the application and asked how to proceed. He advised that what was going on with the application was not too unusual and that he would keep contacting Ms. Barnes to find out when the substitute pages would be forwarded. He said that the application should automatically republish at that time, but we could contact him directly to make sure

that it would. He was in agreement that we had done everything within our power to comply and there should be no legitimate reason as to why there would be more obstacles.

XIX. May 5, 2000. A message was left for Ms. Barnes to ascertain the status of the substitute pages.

XX. May 8, 2000. We spoke with Ms. Barnes, who stated that the documents had not yet reached her and please call her in another week. We asked given that it had been so long since we filed the Response and the fact that it had yet come to her, would it not be easier to have copies of the documents couriered directly to her. She stated that this was not necessary and to call in about a week.

We then contacted Supervisor Carol Bidwell and left a message to find out if there was any way to trace these documents so that they could be expedited to Ms. Barnes.

XXI. May 9, 2000. Ms. Bidwell returned the call. The case history was again outlined for her. We stated that we felt it was suspicious that documents for this particular case kept getting detained where no one seems to be able to locate them. She stated that this is not unusual to take this long for the documents to come to the appropriate person and it was nothing to worry about.

XXII. May 15, 2000. Ms. Barnes states that still no documents have reached her. We insist at this point that given the time constraints, copies of the documents as filed would be couriered directly to her that afternoon. Copies were couriered to her with a cover letter requesting that she contact us when the changes are entered so that we may in turn contact WIPO to arrange for republication.

XXIII. May 26, 2000. Not having heard from Ms. Barnes we contacted her. She stated that the substitute pages were rejected because the drawings had been moved out of the description made into separate formal drawings. We asked her how such a decision could be possible since the Invitation to Correct Defects specifically cited that having the drawings in the description needed to be corrected. We advised her that Ms. Bidwell had even outlined it was in our "best interest" to move these drawings out to bring the application into compliance. At this point, Ms. Barnes stated that she did not have the file in front of her, seemed to be

unfamiliar with exactly what the Invitation to Correct was requesting and stated that she would need to retrieve the file. We referred to our file and read to her verbatim what was entailed on the Invitation to Correct Defects. She requested the name of the person who signed the Invitation, which was given to her at that time. She stated that the decision to refuse the substitute pages had not been made by her, but by Examiner Ho. She again stated that she would need to retrieve the file and requested that we call her back.

XXIV. May 31, 2000. We received an official notification that the substitute pages were rejected. However, no mention was made of this being due to any drawings being moved from the description. The reasoning cited is due to not timely filing the Response to the Invitation to Correct Defects.

XXV. June 5, 2000. We spoke with Ms. Barnes and told her that we were in receipt of the official notification and that no mention was made of the problems she outlined in our May 26 telephone conversation. She seemed puzzled that the factor identified was due to not timely filing the Response. She stated that she had no idea how to tell us to proceed, other than contacting Examiner Ho directly.

On the basis of the difficulties and delays outlined above, we feel that we have done everything within our power to expedite the matter and comply with the requests made by the U.S. PCT Branch in a timely manner. We respectfully request that the substitute pages, which were filed with the Response to Invitation to Correct Defects, and copies of which were again couriered to Ms. Barnes on May 15, 2000, be entered for republication. We further respectfully request, that this Letter of Protest become a part of the official record of the above-identified application at the PCT Branch of the U.S. Patent and Trademark Office.

Respectfully submitted,  
SHANKS & HERBERT

By: David W. Woodward  
David W. Woodward, Reg. No. 35,020

Date: June 16, 2000  
TransPotomac Plaza  
1033 N. Fairfax Street, Suite 306  
Alexandria, VA 22314  
(703) 683-3600

cc: International Bureau of WIPO (via facsimile and courier)

**UNDER THE PATENT COOPERATION TREATY (PCT)  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: Agouron Pharmaceuticals, Inc., et al.

International Appl. No.: PCT/US99/18790

Atty. Docket: 0121-0002PCT

International Filing Date:  
20-August-1999

For: Non-Peptide GnRH Agents, Methods and  
Intermediates For Their Preparation

**RESPONSE TO INVITATION PAY ADDITIONAL FEES**

Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231

Attention: RO/US

Sir:

In response to the Invitation to Pay Additional Fees mailed on 01-June-2000,  
Applicants request that Groups I, II, III, IV, V, VI, and VII all be searched.

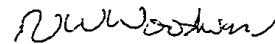
In accordance for examination in these additional groups, Applicants submit the  
following:

1. Copy of Invitation to Pay Additional Fees; and
2. Check in the amount of \$1,260 (for examination of additional groups); and
3. Return postcard.

If the Filing Fee is found to be insufficient for any reason, please charge such deficiency to our Deposit Account No. 50-0622.

Respectfully submitted,

SHANKS & HERBERT



David W. Woodward  
Reg. No.: 35,020

Date: June 12, 2003

TransPotomac Plaza  
1033 N. Fairfax Street  
Suite 306  
Alexandria, VA 22314  
(703) 683-3600

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: TONI-JUNELL HERBERT SHANKS & HERBERT TRANSPOTOMAC PLAZA 1033 NORTH FAIRFAX ST., STE. 306 ALEXANDRIA, VA 22314	<div style="border: 2px solid black; padding: 5px; font-size: 1.5em; font-weight: bold;">DOCKETED</div> <div style="border: 1px solid black; padding: 2px; margin: 2px; font-weight: bold;">JUN 06 2000</div>	<div style="font-size: 1.5em; font-weight: bold;">PCT</div> <div style="font-weight: bold;">INVITATION TO PAY ADDITIONAL FEES</div> <div style="font-weight: bold;">(PCT Article 17(3)(a) and Rule 40.1)</div>
BY <u>CS</u>		Date of Mailing <small>(day/month/year)</small> <b>01 JUN 2000</b>
Applicant's or agent's file reference  0121-0002PCT	<b>PAYMENT DUE</b> within 15 days from the above date of mailing	
International application No.  PCT/US99/18790	International filing date <small>(day/month/year)</small> 20 August 1999 (20.08.1999)	
Applicant  AGOURON PHARMACEUTICALS, INC.		

**1. This International Searching Authority**

(i) considers that there are 7 (number of) inventions claimed in the international application covered by the claims indicated below/on an extra sheet:  
 Please See Continuation Sheet

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below/on an extra sheet:  
 Please See Continuation Sheet

(ii) ☐ has carried out a partial international search (see Annex) ☒ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.: 1-8

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid.

**2. The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:**

<u>\$210.00</u>	X <u>6</u>	= <u>\$1,260.00</u>
Fee additional per invention	number of additional inventions	total amount of additional fees

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☐ Claim(s) Nos. \_\_\_\_\_ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer THOMAS MCKENZIE Telephone No. (703) 308-1235
--	---

JOYCE BRIDGERS  
 PARALEGAL SPECIALIST  
 CHEMICAL MATRIX



INVITATION TO PAY ADDITIONAL FEES

International application No.  
PCT/US 790

This International Search Authority has found 7 inventions claimed in the International Application covered by the claims indicated below:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-8, and claims 9 & 10 in part, drawn to furans.

Group II, claim(s) claims 9 & 10, in part, drawn to pyrroles.

Group III, claim(s) claims 9 & 10, in part, drawn to imidazoles.

Group IV, claim(s) claims 9 & 10, in part, drawn to pyrazoles.

Group V, claim(s) claims 9 & 10, in part, drawn to thiophenes.

Group VI, claim(s) claims 9 & 10, in part, drawn to rings with both nitrogen and oxygen.

Group VII, claim(s) claims 9 & 10, in part, drawn to rings with both nitrogen and sulfur.

This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the five membered ring labeled "het" is the special technical feature seen distinctively in each group. Without this ring, the remaining fragments would be non-novel. If group II is elected, for example, then claims 9 and 10 will be examined to the extent that they read on furans.

RECEIVED

PATENT COOPERATION TREATY

SEP 27 2000

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

SHANKS & HERBERT

PCT

To:  
TONI-JUNELL HERBERT  
SHANKS & HERBERT  
TRANSPOTOMAC PLAZA  
1033 NORTH FAIRFAX ST., STE. 306  
ALEXANDRIA, VA 22314

NOTIFICATION OF RECEIPT  
OF DEMAND BY COMPETENT INTERNATIONAL  
PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence  
and Administrative Instructions, Section 601(a))

Date of mailing  
(day/month/year) 25 SEP 00

Applicant's or agent's file reference  
0121-0002PCT

IMPORTANT NOTIFICATION

International application No. PCT/US99/18790	International filing date (day/month/year) 20 AUG 99	Priority date (day/month/year) 20 AUG 98
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Applicant  
AGOURON PHARMACEUTICALS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

20 MARCH 00

2. That date of receipt is:

- ☒ the actual date of receipt of the demand by this Authority (Rule 61.1(b)).  
☐ the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).  
☐ the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

- ☐ (If applicable) This notification confirms the information given by telephone, facsimile transmission or in person on:

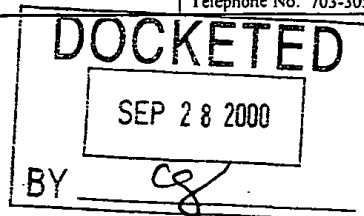
4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/  
Assistant Commissioner for Patent  
Box PCT  
Washington, D.C. 20231 Attn:RO/US  
Facsimile No. 703-305-3230

Authorized officer  
SONYA D. BARNES

Telephone No. 703-305-3665

Form PCT/IPEA/402 (July 1998)



09/763216

JC02 Rec'd PCT/PTO 20 FEB 2001

UNDER THE PATENT COOPERATION TREATY (PCT)  
IN THE UNITED STATES PATENT AND TRADE MARK OFFICE

In re application of: Agouron Pharmaceuticals, Inc.

International Appl. No.: PCT/US99/18790

Atty. Docket: 0121-0002PCT

International Filing Date:  
20-August-1999

For: Non-Peptide GnRH Agents, Methods and  
Intermediates For Their Preparation

RESPONSE TO INVITATION TO RESTRICT OR  
PAY ADDITIONAL FEES

Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231

Attention: RO/US

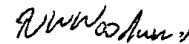
Sir:

In response to the Invitation to Restrict or Pay Additional Fees mailed on 13-  
October-2000, Applicants submit the following:

1. Copy of Invitation to Restrict or Pay Additional Fees; and
2. Check in the amount of \$840 (total amount of charges for six additional  
invention searches).

Respectfully submitted,

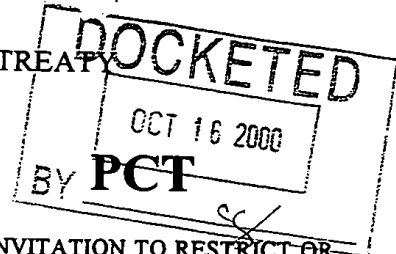
SHANKS & HERBERT



David W. Woodward  
Reg. No.: 35,020

Date: Oct 31 2001  
TransPotomac Plaza  
1033 N. Fairfax Street  
Suite 306  
Alexandria, VA 22314  
(703) 683-3600

# PATENT COOPERATION TREATY



From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: DAVID W. WOODWARD  
SHANKS & HERBERT  
TRANSPOTOMAC PLAZA  
1033 NORTH FAIRFAX ST., STE. 306  
ALEXANDRIA, VA 22314

INVITATION TO RESTRICT OR  
PAY ADDITIONAL FEES

(PCT Article 34(3)(a) and Rule 68.2)

Date of Mailing (day/month/year)      13 OCT 2000	
Applicant's or agent's file reference 0121-0002PCT	REPLY OR PAYMENT DUE within 1 month from the above date of mailing
International application No. PCT/US99/18790	International filing date (day/month/year) 20 AUGUST 1999
Applicant AGOURON PHARMACEUTICALS, INC.	

1. This International Preliminary Examining Authority
  - (i) considers that the international application does not comply with the requirement of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated in the Annex.
  - (ii) therefore considers that there are 7 (number of) inventions claimed in the international application as indicated in the Annex.
  - (iii) recalls that claims relating to inventions in respect of which no international search report has been established need not be the subject of international preliminary examination (Rule 66.1(e)).

2. Consequently the applicant is hereby invited, within the time limit indicated above, to restrict the claims as suggested under item 3 below, or to pay amount indicated below:

\$ 140.00	X 6	= \$ 840.00
Fee additional per invention	number of additional inventions	total amount of additional fees

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. If the applicant opts to restrict the claims, this Authority suggests the restriction possibilities indicated in the Annex, which in its opinion would be in compliance with the requirement of unity of invention.
4. In the absence of any response from the applicant, this Authority will establish the international preliminary examination report on those parts of the international application indicated in the Annex which, in the opinion of this Authority, appear to relate to the main invention.

Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Authorized officer

DEEPAK RAO

Telephone No. (703) 308-1235

Facsimile No. (703) 305-3230

Form PCT/IPEA/405 (July 1992)\*

INVITATION TO RESTRICT OR PAY ADDITIONAL FEES

International application No.

PCT/US99/18790

1. This International Preliminary Examining Authority has found 7 inventions claimed in the International Application covered by the claims indicated below:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 9-10 (in part), drawn to furans.  
Group II, claim(s) 9-10 (in part), drawn to pyrroles.  
Group III, claim(s) 9-10 (in part), drawn to imidazoles.  
Group IV, claim(s) 9-10 (in part), drawn to pyrazoles.  
Group V, claim(s) 9-10 (in part), drawn to thiophenes.  
Group VI, claim(s) 9-10 (in part), drawn to rings with both nitrogen and oxygen.  
Group VII, claim(s) 9-10 (in part), drawn to rings with both nitrogen and sulfur.

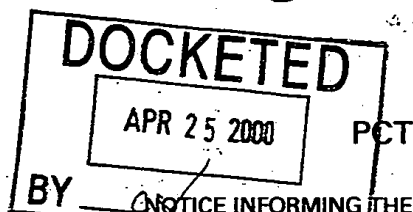
and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I-VII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:  
Groups I-VII relate to structurally dissimilar compounds that lack a common core. The term "het" is defined to be various rings namely furans, imidazoles, pyrazoles, etc., which are not art recognized equivalents. There is no other common special technical feature in the formula which can be considered to constitute a special technical feature defined by PCT Rule 13.2.

4. In the absence of any response from the applicant, this Authority will establish the International Preliminary Examination Report based on the main invention. The claims drawn to the main invention are as follows:

Claims: 1-8 and 9-10 (in part)

PATENT COOPERATION TREATY



**NOTICE INFORMING THE APPLICANT OF THE  
COMMUNICATION OF THE INTERNATIONAL  
APPLICATION TO THE DESIGNATED OFFICES**

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:  
HERBERT, Toni-Junell  
Shanks & Herbert  
TransPotomac Plaza  
Suite 306  
1033 N. Fairfax Street  
Alexandria, VA 22314  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 13 April 2000 (13.04.00)		<b>IMPORTANT NOTICE</b>	
Applicant's or agent's file reference 0121-0002PCT			
International application No. PCT/US99/18790	International filing date (day/month/year) 20 August 1999 (20.08.99)	Priority date (day/month/year) 20 August 1998 (20.08.98)	
Applicant AGOURON PHARMACEUTICALS, INC. et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:  
AU,CN,JP,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:  
AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,EP,ES,FI,GB,GD,GE,GH,GM,  
HR,HU,ID,IL,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,  
RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZA,ZW  
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).
3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 13 April 2000 (13.04.00) under No. WO 00/20358

**REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)**

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

**REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))**

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

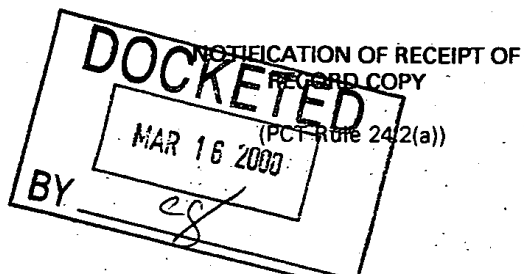
For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU



To:

HERBERT, Toni-Junell  
Shanks & Herbert  
TransPotomac Plaza  
Suite 306  
1033 N. Fairfax Street  
Alexandria, VA 22314  
ÉTATS-UNIS D'AMÉRIQUE

Date of mailing (day/month/year) 03 March 2000 (03.03.00)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference 0121-0002PCT	International application No. PCT/US99/18790

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

AGOURON PHARMACEUTICALS, INC. (for all designated States except US)  
ANDERSON, Mark, Brian et al (for US)

International filing date : 20 August 1999 (20.08.99)  
Priority date(s) claimed : 20 August 1998 (20.08.98)  
Date of receipt of the record copy  
by the International Bureau : 25 February 2000 (25.02.00)

List of designated Offices

AP : GH,GM,KE,LS,MW,SD,SL,SZ,UG,ZW  
EA : AM,AZ,BY,KG,KZ,MD,RU,TJ,TM  
EP : AT,BE,CH,CY,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE  
OA : BF,BJ,CF,CG,CI,CM,GA,GN,GW,ML,MR,NE,SN,TD,TG  
National : AE,AL,AM,AT,AU,AZ,BA,BB,BG,BR,BY,CA,CH,CN,CU,CZ,DE,DK,EE,ES,FI,GB,GD,GE,  
GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KP,KR,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,  
NO,NZ,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,US,UZ,VN,YU,ZA,ZW

**ATTENTION**

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

- ☒ time limits for entry into the national phase  
☒ confirmation of precautionary designations  
☒ requirements regarding priority documents

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer: H. Zhou
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

**INFORMATION ON TIME LIMITS FOR ENTERING THE NATIONAL PHASE**

The applicant is reminded that the "national phase" must be entered before each of the designated Offices indicated in the Notification of Receipt of Record Copy (Form PCT/IB/301) by paying national fees and furnishing translations, as prescribed by the applicable national laws.

The time limit for performing these procedural acts is **20 MONTHS** from the priority date or, for those designated States which the applicant elects in a demand for international preliminary examination or in a later election, **30 MONTHS** from the priority date, provided that the election is made before the expiration of 19 months from the priority date. Some designated (or elected) Offices have fixed time limits which expire even later than 20 or 30 months from the priority date. In other Offices an extension of time or grace period, in some cases upon payment of an additional fee, is available.

In addition to these procedural acts, the applicant may also have to comply with other special requirements applicable in certain Offices. It is the applicant's responsibility to ensure that the necessary steps to enter the national phase are taken in a timely fashion. Most designated Offices do not issue reminders to applicants in connection with the entry into the national phase.

For detailed information about the procedural acts to be performed to enter the national phase before each designated Office, the applicable time limits and possible extensions of time or grace periods, and any other requirements, see the relevant Chapters of Volume II of the PCT Applicant's Guide. Information about the requirements for filing a demand for international preliminary examination is set out in Chapter IX of Volume I of the PCT Applicant's Guide.

GR and ES became bound by PCT Chapter II on 7 September 1996 and 6 September 1997, respectively, and may, therefore, be elected in a demand or a later election filed on or after 7 September 1996 and 6 September 1997, respectively, regardless of the filing date of the international application. (See second paragraph above.)

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

**CONFIRMATION OF PRECAUTIONARY DESIGNATIONS**

This notification lists only specific designations made under Rule 4.9(a) in the request. It is important to check that these designations are correct. Errors in designations can be corrected where precautionary designations have been made under Rule 4.9(b). The applicant is hereby reminded that any precautionary designations may be confirmed according to Rule 4.9(c) before the expiration of 15 months from the priority date. If it is not confirmed, it will automatically be regarded as withdrawn by the applicant. There will be no reminder and no invitation. Confirmation of a designation consists of the filing of a notice specifying the designated State concerned (with an indication of the kind of protection or treatment desired) and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.

**REQUIREMENTS REGARDING PRIORITY DOCUMENTS**

For applicants who have not yet complied with the requirements regarding priority documents, the following is recalled.

Where the priority of an earlier national, regional or international application is claimed, the applicant must submit a copy of the said earlier application, certified by the authority with which it was filed ("the priority document") to the receiving Office (which will transmit it to the International Bureau) or directly to the International Bureau, before the expiration of 16 months from the priority date, provided that any such priority document may still be submitted to the International Bureau before that date of international publication of the international application, in which case that document will be considered to have been received by the International Bureau on the last day of the 16-month time limit (Rule 17.1(a)).

Where the priority document is issued by the receiving Office, the applicant may, instead of submitting the priority document, request the receiving Office to prepare and transmit the priority document to the International Bureau. Such request must be made before the expiration of the 16-month time limit and may be subjected by the receiving Office to the payment of a fee (Rule 17.1(b)).

If the priority document concerned is not submitted to the International Bureau or if the request to the receiving Office to prepare and transmit the priority document has not been made (and the corresponding fee, if any, paid) within the applicable time limit indicated under the preceding paragraphs, any designated State may disregard the priority claim, provided that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity to furnish the priority document within a time limit which is reasonable under the circumstances.

Where several priorities are claimed, the priority date to be considered for the purposes of computing the 16-month time limit is the filing date of the earliest application whose priority is claimed.



# P. ENT COOPERATION TREATY

From the RECEIVING OFFICE

**DOCKETED**

FEB 24 2000

PCT

To:

TONI-JUNELL HERBERT  
SHANKS & HERBERT  
TRANSPOTOMAC PLAZA  
1033 NORTH FAIRFAX ST., STE. 306  
ALEXANDRIA VA 22314

BY CC

NOTIFICATION CONCERNING PAYMENT  
OF PRESCRIBED FEES

(PCT Rules 14, 15 and 16 and Administrative  
Instructions, Sections 304(a) and (b) and 323(b))

Date of mailing  
(day/month/year)

18 FEB 2000

Applicant's or agent's file reference  
0121-0002PCT

PAYMENT DUE

See item 3 for time limits

International application No.

PCT/US99/18790

International filing date/Date of receipt  
(day/month/year)

20 AUG 99

Priority date (day/month/year)

20 AUG 98

Applicant

AGOURON PHARMACEUTICALS, INC.

1. The applicant is hereby notified that this receiving Office has received:

- ☒ the payment of all the prescribed fees, and ☐ an overpayment, which will be refunded in due course.  
☐ no or insufficient payment of the prescribed fees and the applicant is hereby invited to pay the balance due, as summarized under item 2, within the time limit(s) indicated under item 3.

2. Fees and payment calculation:

_____	_____	=	_____
Total fees payable	Amount paid		Balance

☐ The details of the calculation are given in the Annex.

3. Time limit(s) for payment and amount(s) payable (Rules 14.1, 15.4 and 16.1(f)):

- ☐ within ONE MONTH from the date of receipt of the international application (for the transmittal fee (if any), the search fee, the basic fee and the designation fee). The amount payable for each fee is the amount applicable on the date of receipt of the international application.
- ☐ within ONE YEAR from the priority date (only for the designation fee and only if this time limit expires later than the above time limit).  
—If the designation fee is paid within one month from the date of receipt of the international application, the amount payable is the amount applicable on that date of receipt.  
—If the designation fee is paid within one year from the priority date but later than one month from the date of receipt of the international application, the amount payable is the amount applicable on the date of payment. The receiving Office should be consulted for the applicable amount.
- ☐ within 16 MONTHS from the priority date (only for the fee for priority document). The applicant's attention is drawn to the fact that the request made by the applicant under Rule 17.1(b) will be considered not to have been made unless the fee is paid within that time limit.

4. Additional observations (if necessary):

- ☐ The search copy will not be transmitted to the International Searching Authority until the search fee is paid (therefore the start of the international search will be delayed)(Rule 23.1(a) and (b)).

Name and mailing address of the receiving Office  
Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231  
Facsimile No.

Attn: RO/US

Authorized officer

*Georgette Hill*

PCT INTERNATIONAL SERVICES DIVISION

Telephone No.

# PATENT COOPERATION TREATY

From the RECEIVING OFFICE

## PCT

To:

TONI-JUNELL HERBERT  
SHANKS & HERBERT  
TRANSPOTOMAC PLAZA  
1033 NORTH FAIRFAX ST., STE. 306  
ALEXANDRIA VA 22314

NOTIFICATION OF THE INTERNATIONAL  
APPLICATION NUMBER AND OF THE  
INTERNATIONAL FILING DATE

(PCT Rule 20.5(c))

Date of mailing  
(day/month/year)

**18 FEB 2000**

Applicant's or agent's file reference  
**0121-0002PCT**

**IMPORTANT NOTIFICATION**

International application No.

**PCT/US99/18790**

International filing date (day/month/year)

**20 AUG 99**

Priority date (day/month/year)

**20 AUG 98**

Applicant **AGOURON PHARMACEUTICALS, INC.**

Title of the invention **NON-PEPTIDE GNRH AGENTS, METHODS AND INTERMEDIATES  
FOR THEIR PREPARATION**

1. The applicant is hereby notified that the international application has been accorded the international application number and the international filing date indicated above.

2. The applicant is further notified that the record copy of the international application:



was transmitted to the International Bureau on

**18 FEB 2000**



has not yet been transmitted to the International Bureau for the reason indicated below and a copy of this notification has been sent to the International Bureau\*:



because the necessary national security clearance has not yet been obtained.



because (reason to be specified):

\* The International Bureau monitors the transmittal of the record copy by the receiving Office and will notify the applicant (with Form PCT/IB/301) of its receipt. Should the record copy not have been received by the expiration of 14 months from the priority date, the International Bureau will notify the applicant (Rule 22.1(c)).

3. FOREIGN TRANSMITTAL LICENSE INFORMATION

Completed by: *[Signature]*



Additional license for foreign transmittal not required. This subject matter is covered by a license already granted on the equivalent U.S. national application. Refer to that license for information concerning its scope.



License for foreign transmittal not required. 37 CFR 5.11(e)(1) or 37 CFR 5.11(e)(2). However, a license may be required for additional subject matter. See 37 CFR 5.15(b).



Foreign transmittal license granted. 35 U.S.C. 184; 37 CFR 5.11 on **8-30-99:**

(date)



37 CFR 5.15(a)



37 CFR 5.15(b)

Name and mailing address of the receiving Office  
Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231  
Facsimile No.

Attn: RO/US

Authorized officer

*Georgette Hill*

PCT INTERNATIONAL SERVICES DIVISION  
Telephone No.

# PATENT COOPERATION TREATY

From the RECEIVING OFFICE

## PCT

To:

TONI-JUNELL HERBERT  
SHANKS & HERBERT  
TRANSPOTOMAC PLAZA  
1033 NORTH FAIRFAX ST., STE. 306  
ALEXANDRIA VA 22314

INVITATION TO CORRECT DEFECTS IN  
THE INTERNATIONAL APPLICATION

(PCT Articles 3(4)(i) and 14(1) and Rule 26)

Date of mailing  
(day/month/year)

**18 FEB 2000**

Applicant's or agent's file reference  
0121-0002PCT

**REPLY DUE** within **ONE MONTH** from  
the above date of mailing

International application No.  
PCT/US99/18790

International filing date  
(day/month/year) 20 AUG 99

Applicant  
AGOURON PHARMACEUTICALS, INC.

1. ☒ The applicant is hereby invited, within the time limit indicated above, to correct, in the international application as filed, the defects specified on the attached
  - ☒ Annex A
  - ☒ Annex B1 (text matter of the international application as filed)
  - ☐ Annex C1 (drawings of the international application as filed)
2. ☐ The applicant is hereby invited, within the time limit indicated above, to correct, in the translation of the international application furnished under Rule 12.3, the defects specified on the attached
  - ☐ Annex A
  - ☐ Annex B2 (text matter of the translation of the international application)
  - ☐ Annex C2 (drawings of the translation of the international application)

Additional observations (if necessary):

### HOW TO CORRECT THE DEFECTS?

Correction must be submitted by filing a replacement sheet embodying the correction and a letter accompanying the replacement sheet, which shall draw attention to the difference between the replaced sheet and the replacement sheet. A correction may be stated in a letter only if it is of such a nature that it can be transferred from the letter to the record copy without adversely affecting the clarity and direct reproducibility of the sheet onto which the correction is to be transferred (Rule 26.4).

### ATTENTION

Failure to correct the defects will result in the international application being considered withdrawn by this receiving Office (see Rule 26.5 for further details).

A copy of this invitation and any attachments has been sent to the International Bureau  
☒ and the International Searching Authority.

Name and mailing address of the receiving Office  
Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231  
Facsimile No.

Attn: RO/US

Authorized officer

*Georgette Hall*

**PCT INTERNATIONAL SERVICES DIVISION**  
Telephone No.

## ANNEX A TO FORM PCT/RO/106

International application No.

PCT/US99/18790

The receiving Office has found the following defects in the international application:

## 1. As to signature\* of the international application (Rules 4.15 and 90.4), the request:

- a. ☐ is not signed.
- b. ☒ is not signed by all the applicants.
- c. ☐ is not accompanied by the statement referred to in the check list in Box No. VIII of the request explaining the lack of the signature of an applicant for the designation of the United States of America.
- d. ☐ is signed by what appears to be an agent/common representative but
- ☐ the international application is not accompanied by a power of attorney appointing him.
- ☐ the power of attorney accompanying the international application was not signed by all the applicants.

e. ☒ other (specify):

Please give Letter of authority or Resolution  
for the Person who signed the Power of atty.

\* All applicants must sign, including inventors if they are also applicants (e.g. where the United States of America is designated).

## 2. As to indications concerning the applicant, the request (Rules 4.4 and 4.5):

- a. ☐ does not properly indicate the applicant's name (specify):
- b. ☐ does not indicate the applicant's address.
- c. ☐ does not properly indicate the applicant's address (specify):
- d. ☐ does not indicate the applicant's nationality.
- e. ☐ does not indicate the applicant's residence.
- f. ☐ other (specify):

## 3. As to the language of some parts of the international application (Rule 12.1):

- a. ☐ the request is not in (one of) the admitted language(s) which is (are):
- b. ☐ the text matter of the drawings is not in (one of) the admitted language(s) which is (are):
- c. ☐ the abstract is not in (one of) the admitted language(s) which is (are):

## 4. The title of the invention:

- a. ☐ is not indicated in Box No. 1 of the request (Rule 4.1(a)).
- b. ☐ is not indicated at the top of the first sheet of the description (Rule 5.1(a)).
- c. ☐ as appearing in Box No. 1 of the request is not identical with the title heading the description (Rule 5.1(a)).

## 5. As to the abstract (Rule 8):

- ☐ the international application does not contain an abstract.

The physical requirements of the international application are not complied with to the extent which is necessary for the purpose of a reasonably uniform international publication, as specified below (Rule 11). The receiving Office has found the following defects in the presentation of the text matter of the international application:

	Request	Description	Claims	Abstract
a. <input type="checkbox"/> The sheets do not admit of direct reproduction.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. <input type="checkbox"/> The element does not commence on a new sheet.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. <input type="checkbox"/> Sheets are not free from creases, cracks, folds.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. <input type="checkbox"/> Sheets are not used in the upright position.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. <input type="checkbox"/> One side of the sheets is not left unused.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. <input type="checkbox"/> The paper of the sheets is not flexible/strong/white/smooth/non-shiny/durable.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. <input type="checkbox"/> The sheets are not connected as prescribed (Rule 11.4(b)).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. <input type="checkbox"/> Sheets are not A4 size (29.7cm x 21cm).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. <input checked="" type="checkbox"/> The minimum margins on the sheets are not as prescribed (top: 2cm; left side: 2.5cm; right side: 2cm; Bottom: 2cm).		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j. <input type="checkbox"/> The file reference number indicated on the sheets does not appear in the left-hand corner of the sheets, within 1.5 cm of the top of the sheets.		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
k. <input type="checkbox"/> The file reference number exceeds the maximum of 12 characters.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
l. <input type="checkbox"/> The sheets of the description, claims and abstract are not numbered in consecutive Arabic numerals.		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
m. <input type="checkbox"/> The sheet numbers are not centered at the top or bottom of the sheets.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
n. <input checked="" type="checkbox"/> The sheet numbers are in the margin (see i. above for the size of the margins).		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
o. <input type="checkbox"/> The text matter is not typed or printed.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
p. <input type="checkbox"/> The typing on the sheets is not 1½-spaced.		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
q. <input type="checkbox"/> The characters in the text matter on the sheets are less than 0.21 cm high in capital letters.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
r. <input type="checkbox"/> The text matter on the sheets is not in dark, indelible color.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
s. <input checked="" type="checkbox"/> The element contains drawings.	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
t. <input checked="" type="checkbox"/> The sheets contain alterations/overwriting/interlineations/too many erasures.	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
u. <input checked="" type="checkbox"/> The sheets are askew.	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
v. <input checked="" type="checkbox"/> THE SHEETS CONTAIN PHOTO COPY		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Further observations (if necessary):

Page 52, 53, 66 and 70  
 Page 45 thru 51  
 Page 67 and 98  
 Table of compound 1-14 renumbered as 102 thru 115  
 Table of compound 1-62 renumbered as 116-177  
 Table of compound 1-259 renumbered as 178 thru 436  
 100 thru 106 renumbered as 437 thru 442 and abstract as page 44  
 New Pages Required

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF RECEIPT  
OF SEARCH COPY

(PCT Rule 25.1)

To:

TONI-JUNELL HERBERT  
SHANKS & HERBERT  
TRANSPOTOMAC PLAZA  
1033 NORTH FAIRFAX ST., STE. 306  
ALEXANDRIA VA 22314Date of mailing  
(day/month/year)

18 FEB 2000

Applicant's or agent's file reference

0121-0002PCT

## IMPORTANT NOTIFICATION

International application No.

PCT/US99/18790

International filing date (day/month/year)

20 AUG 99

Priority date (day/month/year)

20 AUG 98

Applicant

AGOURON PHARMACEUTICALS, INC.

## 1. Where the International Searching Authority and the receiving Office are not the same Office:

The applicant is hereby notified that the search copy of the international application was received by this International Searching Authority on the date indicated below.

Where the International Searching Authority and the receiving Office are the same Office:

The applicant is hereby notified that the search copy of the international application was received on the date indicated below.

18 FEB 2000

(date of receipt)

## 2. Time limit for establishment of international search report

The applicant is informed that the time limit for establishing the international search report is 3 months from the date of receipt indicated above or 9 months from the priority date, whichever time limit expires later.

## 3. A copy of this notification has been sent to the International Bureau and, where the first sentence of paragraph 1 applies, to the receiving Office.

Name and mailing address of the ISA/US  
Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231  
Facsimile No.

Attn: ISA/US

Authorized officer

Georgios H. H.  
PCT INTERNATIONAL SEARCH DIVISION  
Telephone No.

TO

TONI-JUNELL HERBERT  
SHANKS & HERBERT  
TRANSPOTOMAC PLAZA  
1033 NORTH FAIRFAX ST., STE. 306  
ALEXANDRIA VA 22314

UNITED STATES DESIGNATED/ELECTED  
OFFICE (DO/EO/US)...

NOTIFICATION OF STATUS OF  
REQUIREMENTS UNDER 35 U.S.C. 371

DATE OF MAILING

18 FEB 2000

FILE REFERENCE

0121-0002PCT

## IDENTIFICATION OF INTERNATIONAL APPLICATION

International Application Number	International Filing Date	Priority Date Claimed
PCT/US99/18790	20 AUG 99	20 AUG 98

Applicant for DO/EO/US

*Anderson, Mark Brian*

## NOTIFICATION

The applicant is hereby advised that the U.S. Patent and Trademark Office in its capacity as ☐ Designated Office ☒ Elected Office has received the following items as of the date of mailing indicated above.

1. ☐ U.S. National fee [35 U.S.C.371 (c) (1)]
  2. ☐ Oath of declaration [35 U.S.C.371 (c) (4)]
  3. ☒ Copy of International application as filed [35 U.S.C.371 (c) (2)]
  4. ☐ Translation of Application [35 U.S.C.371 (c) (2)]
  5. ☐ Amendments under PCT Article 19 [35 U.S.C.371 (c) (3)]
  6. ☐ Translation of PCT Article 19 Amendments [35 U.S.C.371 (c) (3)]
  7. ☐ Search Report or Declaration under PCT Article 17(2) [35 U.S.C.371 (a)]
  8. ☐ International Preliminary Examination Report and its Annexes, if any, under PCT Article 36(3) (a) [35 U.S.C.371 (a)]
  9. ☐ Translation of Annexes to the International Preliminary Examination Report under PCT Article 36(3) (b) [35 U.S.C.371 (c) (5)]
  10. ☐ Other items received:
    - ☐ Assignment Document ☐ Prior Art Statement ☐ Preliminary Amendment
- A. ☐ Requirements for U.S. National processing have been met. Processing will commence
- ☐ at the expiration of the applicable time limit under either
    - ☐ PCT Article 22 [35 U.S.C.371 (b)] or
    - ☐ PCT Article 39 [35 U.S.C.371 (b)]
  - ☐ on the date indicated below under the provisions of 35 U.S.C.371 (f)

U.S. NATIONAL SERIAL#

DATE UNDER 35 U.S.C.102(e)

DATE OF COMMENCEMENT OF  
NATIONAL PROCESSING

All correspondence submitted after the date of commencement of U.S. National processing indicated above should refer to the U.S. National Serial Number and the appropriate U.S. National processing organization or Officer.

- B. ☐ As the above identified application has been accepted for U.S. National processing under the provisions of 35 U.S.C.371 (f) before expiration of the applicable time limit under ☐ PCT Article 22 ☐ PCT Article 39, applicant is reminded that
- ☐ Amendments under PCT Article 19 and/or
  - ☐ the International Preliminary Examination Report and its Annexes, if any, under PCT Article 36(3) (a), and (b)
- and any translation thereof, if applicable, must be submitted to the Patent and Trademark Office as soon as they are available.

International application No. <u>708 39 / 19790</u>	International filing date <u>20 AUG 1998</u>	Priority Date Claimed <u>20 AUG 1998</u>
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- C. ☒ In order that U.S. National processing may begin, certain items must be received by the DO/EO/US by the expiration of applicable time limit under
- ☒ PCT Article 22 or
  - ☒ PCT Article 39.
- Specifically:
- ☒ 1. U.S. National Fee
  - ☒ 2. Oath or Declaration
  - ☐ 3. Copy of Application
  - ☐ 4. Translation of application
  - ☒ 5. Amendments under PCT Article 19, if any
  - ☐ 6. Translation of PCT Article 19 Amendments, if applicable
  - ☐ 7. Search Report or PCT Article 17(2) declaration
  - ☐ 8. International Preliminary Examination Report and its Annexes, if any, under PCT Article 36(3)(a), if applicable
  - ☐ 9. Translation of Annexes to the International Preliminary Examination Report under PCT Article 36(3)(b), if applicable

**THE ABOVE CHECK ITEMS MUST BE TIMELY RECEIVED TO AVOID ABANDONMENT OF THE APPLICATION.**  
**[35. U.S.C. 371(d)]**

D. Further information for the applicant:

**This is only a reminder.**

**UNITED STATES DESIGNATED/ELECTED OFFICE**

Address Only:  
 Assistant Commissioner for Patent  
 Box PCT  
 Washington, D.C. 20231 Attn: RO/US

Authorized Officer Georgette Hill  
**PCT INTERNATIONAL SERVICES DIVISION**



## UNITED STATES RECEIVING OFFICE(RO/US) FEE CODING AND RECORDING SHEET

☐ ADDL  
SHEETS

## IDENTIFICATION OF THE INTERNATIONAL APPLICATION

INTERNATIONAL APPLICATION NUMBER

INTERNATIONAL FILING DATE

PCT/US 99/18790

20 AUG 1999

APPLICANT (Name)

## PAYMENTS

## REFUNDS

Payment on Filing				Deposit Account		Deposit Account		To Deposit Account		To Deposit Account	
				DATE:		DATE:		DATE:		DATE:	
Deposit Account				DATE:		DATE:		DATE:		DATE:	
<input type="checkbox"/> CASH/CHECK				<input type="checkbox"/> CASH/CHECK		<input type="checkbox"/> CASH/CHECK		<input type="checkbox"/> BY CHECK		<input type="checkbox"/> BY CHECK	
150											
151											
153											
800											
801											
802											
899											
866											
Total Paid:				Total Paid:		Total Paid:		Total Refunded:		Total Refunded:	
States Included for 892:				892:		892:					
States Included for 893:				893:		893:					

CALCULATED FEE AMOUNT =

AMOUNT OF DIFFERENCE =

08/24/1999 KDUNCAM1 0000099\_PCT/US99/18790

01 FC:150	240.00 OP
02 FC:151	700.00 OP
03 FC:800	455.00 OP
04 FC:801	4200.00 OP
05 FC:899	1050.00 OP
06 FC:866	15.00 OP

RO/US Authorization

RO/US Authorization

RO/US Authorization

RO/US Authorization

RO/US Authorization

PCT/RO/192(6) (U.S. VERSION)  
(Rev. 07-92)

U.S. DEPARTMENT OF COMMERCE - Patent and Trademark Office

## PATENT COOPERATION TREATY

PCT

INFORMATION CONCERNING ELECTED  
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

From the INTERNATIONAL BUREAU

To:

HERBERT, Toni-Junell  
Shanks & Herbert  
TransPotomac Plaza  
Suite 306  
1033 N. Fairfax Street  
Alexandria, VA 22314  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 29 September 2000 (29.09.00)		
Applicant's or agent's file reference 0121-0002PCT		IMPORTANT INFORMATION
International application No. PCT/US99/18790	International filing date (day/month/year) 20 August 1999 (20.08.99)	
Applicant AGOURON PHARMACEUTICALS, INC. et al		Priority date (day/month/year) 20 August 1998 (20.08.98)

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

AP : GH,GM,KE,LS,MW,SD,SL,SZ,UG,ZW  
EP : AT,BE,CH,CY,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE  
National : AU,BG,CA,CN,CZ,DE,IL,JP,KP,KR,MN,NO,NZ,PL,RO,RU,SE,SK,US

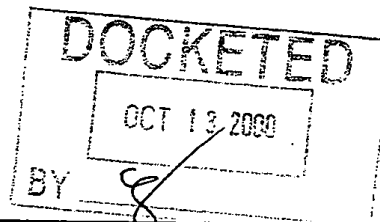
2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

EA : AM,AZ,BY,KG,KZ,MD,RU,TJ,TM  
OA : BF,BJ,CF,CG,CI,CM,GA,GN,GW,ML,MR,NE,SN,TD,TG  
National : AE,AL,AM,AT,AZ,BA,BB,BR,BY,CH,CU,DK,EE,ES,FI,GB,GD,GE,GH,GM,HR,  
HU,ID,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MW,MX,PT,SD,SG,SI,SL,  
TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZA,ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent.



The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. (41-22) 740.14.35	Authorized officer:  H. Zhou  Telephone No. (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

**NOTIFICATION CONCERNING  
THE FILING OF AMENDMENTS OF THE CLAIMS**  
(PCT Administrative Instructions, Section 417)

From the INTERNATIONAL BUREAU

To:

HERBERT, Toni-Junell  
Shanks & Herbert  
TransPotomac Plaza  
Suite 306  
1033 N. Fairfax Street  
Alexandria, VA 22314  
ETATS-UNIS D'AMERIQUE

<b>Date of mailing</b> (day/month/year)	23 October 2000 (23.10.00)
<b>Applicant's or agent's file reference</b>	0121-0002PCT
<b>International application No.</b>	PCT/US99/18790
<b>Applicant</b>	AGOURON PHARMACEUTICALS, INC. et al
<b>International filing date</b> (day/month/year)	20 August 1999 (20.08.99)
<b>IMPORTANT NOTIFICATION</b>	

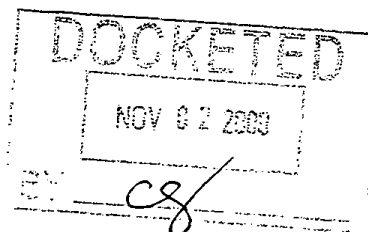
1. The applicant is hereby notified that amendments to the claims under Article 19 were received by the International Bureau on:

20 October 2000 (20.10.00)

2. This date is within the time limit under Rule 46.1.

Consequently, the international publication of the international application will contain the amended claims according to Rule 48.2(f), (h) and (i).

3. The applicant is reminded that the international application (description, claims and drawings) may be amended during the international preliminary examination under Chapter II, according to Article 34, and in any case, before each of the designated Offices, according to Article 28 and Rule 52, or before each of the elected Offices, according to Article 41 and Rule 78.



<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorised officer</p> <p align="center">H. Zhou</p> <p>Telephone No.: (41-22) 338.83.38</p>
--	---

TRANSMITTAL LETTER TO THE  
UNITED STATES RECEIVING OFFICE

Date	20-August-1999
International Application No.	To Be Assigned
Attorney Docket No.	0121-0002PCT

I. Certification under 37 CFR 1.10 (if applicable)

Express Mail mailing number
-----------------------------

Date of Deposit
-----------------

I hereby certify that the application/correspondence attached hereto is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Assistant Commissioner for Patents, Washington, D.C. 20231.

Signature of person mailing correspondence
--

Typed or printed name of person mailing correspondence
--

II. ☒ New International Application

TITLE	Non-Peptide GnRH Agents, Methods and Intermediates for Their Preparation
-------	--

Earliest priority date (Day/Month/Year)
20-August-1998

**SCREENING DISCLOSURE INFORMATION:** In order to assist in screening the accompanying international application for purposes of determining whether a license for foreign transmittal should and could be granted and for other purposes, the following information is supplied. (Note: check as many boxes as apply):

- A. ☐ The invention disclosed was not made in the United States.
- B. ☐ There is no prior U.S. application relating to this invention.
- C. ☒ The following prior U.S. application(s) contain subject matter which is related to the invention disclosed in the attached international application. (NOTE: priority to these applications may or may not be claimed on form PCT/RO/101 (Request) and this listing does not constitute a claim for priority).

application no.	60/097,520	filed on	20-August-1998
application no.		filed on	

- D. ☐ The present international application ☐ is identical ☐ contains less subject matter than that found in the prior U.S. application(s) identified in paragraph C.
- E. ☒ The present international application ☒ contains additional subject matter not found in the prior U.S. application(s) identified in paragraph C. above. The additional subject matter is found on pages all and ☒ DOES NOT ALTER ☐ MIGHT BE CONSIDERED TO ALTER the general nature of the invention in a manner which would require the U.S. application to have been made available for inspection by the appropriate defense agencies under 35 U.S.C. 181 and 37 CFR 5.1. See 37 CFR 5.15

III. ☐ A Response to an Invitation from the RO/US. The following document(s) is (are) enclosed:

- A. ☐ A Request for An Extension of Time to File a Response
- B. ☐ A Power of Attorney (General or Regular)
- C. ☐ Replacement pages:

pages		of the request (PCT/RO/101)	pages		of the figures
pages		of the description	pages		of the abstract
pages		of the claims			

- D. ☐ Submission of Priority Documents

Priority document		Priority document	
-------------------	--	-------------------	--

- E. ☐ Fees as specified on attached Fee Calculation sheet form PCT/RO/101 annex

IV. ☐ A Request for Rectification under PCT 91 ☐ A Petition ☐ A Sequence Listing Diskette

V. ☐ Other (please specify):

The person  
signing this  
form is the:

- ☐ Applicant
- ☒ Attorney/Agent (Reg. No.)  
35,020
- ☐ Common Representative

David W. Woodward

Typed name of signer

*David W. Woodward*

Signature

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) 0121-0002PCT

<b>Box No. I TITLE OF INVENTION</b> Non-Peptide GnRH Agents, Methods and Intermediates for Their Preparation	
<b>Box No. II APPLICANT</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) Agouron Pharmaceuticals, Inc. 10350 North Torrey Pines Road La Jolla, California 92037 United States of America	
<input type="checkbox"/> This person is also inventor.	
Telephone No.	
Facsimile No.	
Teleprinter No.	
State (that is, country) of nationality: US	State (that is, country) of residence: US
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input checked="" type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<b>Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) ANDERSON, Mark Brian 41 Las Cascadas Orinda, California 94563 United States of America	
This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)	
State (that is, country) of nationality: US	State (that is, country) of residence: US
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<input checked="" type="checkbox"/> Further applicants and/or (further) inventors are indicated on a continuation sheet.	
<b>Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE</b>	
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: <input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) HERBERT, Toni-Junell SHANKS & HERBERT TransPotomac Plaza 1033 North Fairfax Street, Suite 306 Alexandria, Virginia 22314 United States of America	
Telephone No. 703-683-3600	
Facsimile No. 703-683-9875	
Teleprinter No.	
<input type="checkbox"/> Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.	

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTOR(S)	
<i>If none of the following sub-boxes is used, this sheet is not to be included in the request.</i>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) VAZIR, Haresh N. 10528 Caminito Pollo San Diego, California 92126 United States of America	This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: US	State (that is, country) of residence: US
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) LUTHIN, David Robert 1772 Shadow Mountain Drive Encinitas, California 92024 United States of America	This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: US	State (that is, country) of residence: US
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) PADERES, Genevieve DeGuzman 5183 Sea Mist Court San Diego, California 92121 United States of America	This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: US	State (that is, country) of residence: US
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) PATHAK, Ved P. 4140-157 Via Candidiz San Diego, California 92130 United States of America	This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: Canada	State (that is, country) of residence: US
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<input type="checkbox"/> Further applicants and/or (further) inventors are indicated on another continuation sheet.	

## Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTOR(S)

*If none of the following sub-boxes is used, this sheet is not to be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) CHRISTIE, Lance Christopher 518 Mynah Place Vista, California 92083 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: US	State (that is, country) of residence: US	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) HONG, Yufeng 11980 Ashley Place San Diego, California 92128 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: China	State (that is, country) of residence: US	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) TOMPKINS, Eileen Valenzuela 10129 West Lilac Road Escondido, California 92026 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: US	State (that is, country) of residence: US	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) LI, Haitao 9699 Palmilla Drive #3112 San Diego, California 92122 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: China	State (that is, country) of residence: US	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
<input type="checkbox"/> Further applicants and/or (further) inventors are indicated on another continuation sheet.		

## Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

FAUST, James  
15684 Bernardo Center Drive #2010  
San Diego, California 92127  
United States of America

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
US

State (that is, country) of residence:  
US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.



**Box No.V DESIGNATION OF STATES**

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

**Regional Patent**

- ☒ **AP** ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA** Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of
- ☒ **EP** European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA** OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

**National Patent (if other kind of protection or treatment desired, specify on dotted line):**

- |   |   |
|---|---|
| <input checked="" type="checkbox"/> <b>AE</b> United Arab Emirates                  | <input checked="" type="checkbox"/> <b>LR</b> Liberia                                   |
| <input checked="" type="checkbox"/> <b>AL</b> Albania                               | <input checked="" type="checkbox"/> <b>LS</b> Lesotho                                   |
| <input checked="" type="checkbox"/> <b>AM</b> Armenia                               | <input checked="" type="checkbox"/> <b>LT</b> Lithuania                                 |
| <input checked="" type="checkbox"/> <b>AT</b> Austria                               | <input checked="" type="checkbox"/> <b>LU</b> Luxembourg                                |
| <input checked="" type="checkbox"/> <b>AU</b> Australia                             | <input checked="" type="checkbox"/> <b>LV</b> Latvia                                    |
| <input checked="" type="checkbox"/> <b>AZ</b> Azerbaijan                            | <input checked="" type="checkbox"/> <b>MD</b> Republic of Moldova                       |
| <input checked="" type="checkbox"/> <b>BA</b> Bosnia and Herzegovina                | <input checked="" type="checkbox"/> <b>MG</b> Madagascar                                |
| <input checked="" type="checkbox"/> <b>BB</b> Barbados                              | <input checked="" type="checkbox"/> <b>MK</b> The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> <b>BG</b> Bulgaria                              |   |
| <input checked="" type="checkbox"/> <b>BR</b> Brazil                                | <input checked="" type="checkbox"/> <b>MN</b> Mongolia                                  |
| <input checked="" type="checkbox"/> <b>BY</b> Belarus                               | <input checked="" type="checkbox"/> <b>MW</b> Malawi                                    |
| <input checked="" type="checkbox"/> <b>CA</b> Canada                                | <input checked="" type="checkbox"/> <b>MX</b> Mexico                                    |
| <input checked="" type="checkbox"/> <b>CH and LI</b> Switzerland and Liechtenstein  | <input checked="" type="checkbox"/> <b>NO</b> Norway                                    |
| <input checked="" type="checkbox"/> <b>CN</b> China                                 | <input checked="" type="checkbox"/> <b>NZ</b> New Zealand                               |
| <input checked="" type="checkbox"/> <b>CU</b> Cuba                                  | <input checked="" type="checkbox"/> <b>PL</b> Poland                                    |
| <input checked="" type="checkbox"/> <b>CZ</b> Czech Republic                        | <input checked="" type="checkbox"/> <b>PT</b> Portugal                                  |
| <input checked="" type="checkbox"/> <b>DE</b> Germany                               | <input checked="" type="checkbox"/> <b>RO</b> Romania                                   |
| <input checked="" type="checkbox"/> <b>DK</b> Denmark                               | <input checked="" type="checkbox"/> <b>RU</b> Russian Federation                        |
| <input checked="" type="checkbox"/> <b>EE</b> Estonia                               | <input checked="" type="checkbox"/> <b>SD</b> Sudan                                     |
| <input checked="" type="checkbox"/> <b>ES</b> Spain                                 | <input checked="" type="checkbox"/> <b>SE</b> Sweden                                    |
| <input checked="" type="checkbox"/> <b>FI</b> Finland                               | <input checked="" type="checkbox"/> <b>SG</b> Singapore                                 |
| <input checked="" type="checkbox"/> <b>GB</b> United Kingdom                        | <input checked="" type="checkbox"/> <b>SI</b> Slovenia                                  |
| <input checked="" type="checkbox"/> <b>GD</b> Grenada                               | <input checked="" type="checkbox"/> <b>SK</b> Slovakia                                  |
| <input checked="" type="checkbox"/> <b>GE</b> Georgia                               | <input checked="" type="checkbox"/> <b>SL</b> Sierra Leone                              |
| <input checked="" type="checkbox"/> <b>GH</b> Ghana                                 | <input checked="" type="checkbox"/> <b>TJ</b> Tajikistan                                |
| <input checked="" type="checkbox"/> <b>GM</b> Gambia                                | <input checked="" type="checkbox"/> <b>TM</b> Turkmenistan                              |
| <input checked="" type="checkbox"/> <b>HR</b> Croatia                               | <input checked="" type="checkbox"/> <b>TR</b> Turkey                                    |
| <input checked="" type="checkbox"/> <b>HU</b> Hungary                               | <input checked="" type="checkbox"/> <b>TT</b> Trinidad and Tobago                       |
| <input checked="" type="checkbox"/> <b>ID</b> Indonesia                             | <input checked="" type="checkbox"/> <b>UA</b> Ukraine                                   |
| <input checked="" type="checkbox"/> <b>IL</b> Israel                                | <input checked="" type="checkbox"/> <b>UG</b> Uganda                                    |
| <input checked="" type="checkbox"/> <b>IN</b> India                                 | <input checked="" type="checkbox"/> <b>US</b> United States of America                  |
| <input checked="" type="checkbox"/> <b>IS</b> Iceland                               |   |
| <input checked="" type="checkbox"/> <b>JP</b> Japan                                 | <input checked="" type="checkbox"/> <b>UZ</b> Uzbekistan                                |
| <input checked="" type="checkbox"/> <b>KE</b> Kenya                                 | <input checked="" type="checkbox"/> <b>VN</b> Viet Nam                                  |
| <input checked="" type="checkbox"/> <b>KG</b> Kyrgyzstan                            | <input checked="" type="checkbox"/> <b>YU</b> Yugoslavia                                |
| <input checked="" type="checkbox"/> <b>KP</b> Democratic People's Republic of Korea | <input checked="" type="checkbox"/> <b>ZA</b> South Africa                              |
|   | <input checked="" type="checkbox"/> <b>ZW</b> Zimbabwe                                  |
- Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:
- ☐ .....
- ☐ .....

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

**Supplemental Box**
*If the Supplemental Box is not used, this sheet need not be included in the request.*

1. If, in any of the Boxes, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:

- (i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;
- (iv) if, in addition to the agent(s) indicated in Box IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V., the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;
- (vi) if, in Box No. VI, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;
- (vii) if, in Box No. VI, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed.

2. If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.

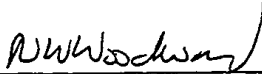
3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.

Continuation of Box No. IV

WOODWARD, David W.  
SHANKS & HERBERT  
TransPotomac Plaza  
1033 North Fairfax Street, Suite 306  
Alexandria, Virginia 22314  
United States of America  
703-683-3600  
703-683-9875 (facsimile)

and

EVANS, Linda S.  
Agouron Pharmaceuticals, Inc.  
Legal Department  
10350 North Torrey Pines Road  
La Jolla, California 92037  
858-622-3000  
858-622-3297 (facsimile)

<b>Box No. VI PRIORITY CLAIM</b>		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application:* regional Office	international application: receiving Office
item (1) 20-August-1998 20-08-98	60/097,520	US		
item (2)				
item (3)				
<input checked="" type="checkbox"/> The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): <u>1</u> <small>* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.</small>				
<b>Box No. VII INTERNATIONAL SEARCHING AUTHORITY</b>				
Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):		Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):		
ISA/ us		Date (day/month/year)      —Number—      Country (or regional Office)		
<b>Box No. VIII CHECK LIST: LANGUAGE OF FILING</b>				
This international application contains the following number of sheets:		This international application is accompanied by the item(s) marked below:		
request :	7	1. <input checked="" type="checkbox"/> fee calculation sheet		
description (excluding sequence listing part) :	439	2. <input type="checkbox"/> separate signed power of attorney		
claims :	3	3. <input checked="" type="checkbox"/> copy of general power of attorney; reference number, if any:		
abstract :	1	4. <input type="checkbox"/> statement explaining lack of signature		
drawings :		5. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s):		
sequence listing part of description :		6. <input type="checkbox"/> translation of international application into (language):		
Total number of sheets :	450	7. <input type="checkbox"/> separate indications concerning deposited microorganism or other biological material		
		8. <input type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form		
		9. <input checked="" type="checkbox"/> other (specify): transmittal letter, check and postcards		
Figure of the drawings which should accompany the abstract:		Language of filing of the international application: English		
<b>Box No. IX SIGNATURE OF APPLICANT OR AGENT</b>				
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request):				
 David W. Woodward Agent for Applicant				

For receiving Office use only		2. Drawings:  <input type="checkbox"/> received:  <input type="checkbox"/> not received:
1. Date of actual receipt of the purported international application:		
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority (if two or more are competent): ISA/	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid	

For International Bureau use only
Date of receipt of the record copy by the International Bureau:

This sheet is not part of and does not count as a sheet of the international application.

# PCT

## FEE CALCULATION SHEET Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's  
file reference

0121-0002PCT

Applicant  
Agouron Pharmaceuticals, Inc.

### CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE	240.00	T
2. SEARCH FEE	700.00	S
International search to be carried out by <u>US</u>		
(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)		
3. INTERNATIONAL FEE		
Basic Fee		
The international application contains <u>450</u> sheets.		
first 30 sheets	455.00	b <sub>1</sub>
<u>420</u> remaining sheets	x <u>\$10.00</u> additional amount	= <u>4,200.00</u> b <sub>2</sub>
Add amounts entered at b <sub>1</sub> and b <sub>2</sub> and enter total at B	4,655.00	B
Designation Fees		
The international application contains <u>78</u> designations.		
<u>10</u> number of designation fees payable (maximum 10)	x <u>105.00</u> amount of designation fee	= <u>1,050.00</u> D
Add amounts entered at B and D and enter total at I	5,705.00	I
(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D)		
4. FEE FOR PRIORITY DOCUMENT (if applicable)	15.00	P
5. TOTAL FEES PAYABLE	6,660.00	
Add amounts entered at T, S, I and P, and enter total in the TOTAL box	TOTAL	

☐ The designation fees are not paid at this time.

### MODE OF PAYMENT

<input type="checkbox"/> authorization to charge deposit account (see below)	<input type="checkbox"/> bank draft	<input type="checkbox"/> coupons
<input checked="" type="checkbox"/> cheque	<input type="checkbox"/> cash	<input type="checkbox"/> other (specify):
<input type="checkbox"/> postal money order	<input type="checkbox"/> revenue stamps	

### DEPOSIT ACCOUNT AUTHORIZATION (this mode of payment may not be available at all receiving Offices)

The RO/ US ☐ is hereby authorized to charge the total fees indicated above to my deposit account.

☒ (this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

☐ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

50-0622  
Deposit Account Number

August 20, 1992  
Date (day/month/year)

N. W. Schubert  
Signature

This sheet is not part of and does not count as a sheet of the international application.

# PCT

## FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's  
file reference

0121-0002PCT

Applicant  
Agouron Pharmaceuticals, Inc.

### CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE	240.00	T
2. SEARCH FEE	700.00	S
International search to be carried out by <u>US</u>		
(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)		
3. INTERNATIONAL FEE		
Basic Fee		
The international application contains <u>450</u> sheets.		
first 30 sheets	455.00	b <sub>1</sub>
<u>420</u> x <u>\$10.00</u>	=	<u>4,200.00</u> b <sub>2</sub>
remaining sheets additional amount		
Add amounts entered at b <sub>1</sub> and b <sub>2</sub> and enter total at B	4,655.00	B
Designation Fees		
The international application contains <u>78</u> designations.		
<u>10</u> x <u>105.00</u>	=	<u>1,050.00</u> D
number of designation fees amount of designation fee payable (maximum 10)		
Add amounts entered at B and D and enter total at I	5,705.00	I
(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and		
4. FEE FOR PRIORITY DOCUMENT (if applicable)	15.00	P
5. TOTAL FEES PAYABLE	6,660.00	
Add amounts entered at T, S, I and P, and enter total in the TOTAL box	TOTAL	

☐ The designation fees are not paid at this time.

### MODE OF PAYMENT

<input type="checkbox"/> authorization to charge deposit account (see below)	<input type="checkbox"/> bank draft	<input type="checkbox"/> coupons
<input checked="" type="checkbox"/> cheque	<input type="checkbox"/> cash	<input type="checkbox"/> other (specify):
<input type="checkbox"/> postal money order	<input type="checkbox"/> revenue stamps	

### DEPOSIT ACCOUNT AUTHORIZATION (this mode of payment may not be available at all receiving Offices)

The RO/ US ☐ is hereby authorized to charge the total fees indicated above to my deposit account.

☒ (this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

☐ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

50-0622

Deposit Account Number

Date (day/month/year)

Signature

PCT

GENERAL POWER OF ATTORNEY

(for several international applications filed under the Patent Cooperation Treaty)

(PCT Rule 90.5)

The undersigned person(s):

(Family name followed by given name; for a full legal entity, full official designation. The address must include postal code and name of country.)

Agouron Pharmaceuticals, Inc.  
10350 North Torrey Pines Road  
La Jolla, California 92037-1022  
United States of America

hereby appoints the following person as

☒ agent

☐ common representative

Name and address

(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

Herbert, Toni-Junell and  
Woodward, David W.  
Shanks & Herbert  
TransPotomac Plaza  
1033 North Fairfax Street, Suite 306  
Alexandria, Virginia 22314  
United States of America

Evans, Linda S.  
Agouron Pharmaceuticals, Inc.  
Legal Department  
10350 North Torrey Pines Road  
La Jolla, California 92037-1022  
United States of America

to represent the undersigned before

☒ all the competent International Authorities

☐ the International Searching Authority only

☐ the International Preliminary Examining Authority only

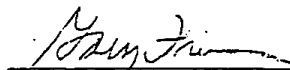
in connection with any and all international applications filed by the undersigned with the following Office

United States

designating Office

and to make or receive payments on behalf of the undersigned

Signature(s) where there are several persons, each of them must sign; next to each signature, indicate the name of the person signing and the capacity in which the person signs, if such capacity is not obvious from reading this power

  
Cory Friedman  
Corporate Vice-President and General Counsel  
Agouron Pharmaceuticals, Inc.

Date 9 July 1999

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

## PCT

### NOTIFICATION OF DECISION CONCERNING REQUEST FOR RECTIFICATION

(PCT Rule 91.1(f))

To:

TONY-JUNELL HERBERT  
SHANKS & HERBERT  
TRANSPOTOMAC PLAZA  
1033 NORTH FAIRFAX STREET  
SUITE 306  
ALEXANDRIA, VA 22314

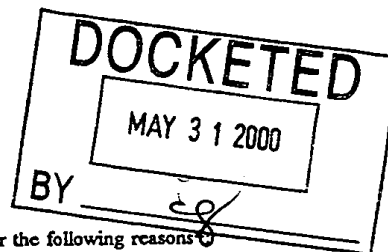
Date of Mailing (day/month/year)	<b>25 MAY 2000</b>
Applicant's or agent's file reference <b>0121-0002PCT</b>	REPLY DUE <div style="text-align: center;">NONE However, see last paragraph below</div>
International application No. <b>PCT/US99/18790</b>	International filing date (day/month/year) <b>20 AUGUST 1999</b>

Applicant  
**AGOURON PHARMACEUTICALS, INC.**

The applicant is hereby notified that this International Searching Authority has considered the request for rectification of obvious errors in the international application/in other papers submitted by the applicant to this Authority, and that it has decided:

1. ☐ to authorize the rectification:
- ☐ as requested by the applicant.  
☐ to the extent set forth below\*:  
 (see continuation sheet)

2. ☒ to refuse to authorize the rectification or part of it for the following reasons:
- (see continuation sheet)



A copy of this notification, together with a copy of the applicant's request for rectification, has been sent to the receiving Office and to the International Bureau.

- \* If the authorization of the rectification has been refused in whole or in part, the applicant may request the International Bureau, before the technical preparations for international publication have been completed and subject to the payment of a fee, to publish the request for rectification together with the international application. See Rule 91.1(f), third and fourth sentences, and, for the amount of the fee, see Annex B2(WO), Volume I of the PCT Applicant's Guide.

Name and mailing address of the ISA/US  
Assistant Commissioner for Patents  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 308-6459

Authorized officer

Nguyen Ngoc-Hoi

Telephone No. (703) 308-6508

NOTIFICATION OF DECISION CONCERNING  
REQUEST FOR RECTIFICATION

International application No.

PCT/US99/18790

2. Applicants request for rectification of obvious errors has been refused for the following reasons:

This International Searching Authority has considered applicant's communication filed 15 May 2000 and has decided to refuse entry of all offered replacement sheets of description, claims, abstract and drawings because the submission of these sheets was untimely.

Under PCT Rule 91.1(g)(i) the authorization for rectification shall be effective only "if its notification to the International Bureau reaches that Bureau before the expiration of 17 months from the priority date." Applicant's request for rectification was received in the Receiving Office after the expiration of 17 months from the priority date.

Accordingly, the offered rectified sheets will not be entered.

Applicant may resubmit these changes to the description, claims, abstract and drawings as Amendments under PCT Article 34 with the Demand when entering Chapter II proceedings under the provisions of the Treaty or may resubmit the changes for entry into the national stage.



# PATENT COOPERATION TREATY

**DOCKETED**

AUG 21 2000

AUG 21 2000

SHANKS & HERBERT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
TONI-JUNELL HERBERT  
SHANKS & HERBERT  
TRANSPOTOMAC PLAZA  
1033 NORTH FAIRFAX ST., STE. 306  
ALEXANDRIA, VA 22314

(PCT Rule 44.1)

Applicant's or agent's file reference 0121-0002PCT	Date of Mailing (day/month/year) <b>21 AUG 2000</b>
International application No. PCT/US99/18790	International filing date (day/month/year) 20 AUGUST 1999 (20.08.1999)
Applicant AGOURON PHARMACEUTICAL, INC.	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.  
 Filing of amendments and statement under Article 19:  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompany sheet.

**Where?** Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau.  
 If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Mark Berch, Ph.D. Telephone No. (703) 308-1235
--	---

Form PCT/ISA/220 (July 1998)

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 0121-0002PCT	<b>FOR FURTHER ACTION</b>	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US99/18790	International filing date (day/month/year) 20 AUGUST 1999 (20.08.1999)	(Earliest) Priority Date (day/month/year) 20 AUGUST 1998 (20.8.98)
Applicant AGOURON PHARMACEUTICAL, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

#### 1. Basis of the Report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☒ Unity of invention is lacking (See Box II).

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

Please See Continuation Sheet

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/18790

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/18790

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/34, 31/505, 31/50; C07D 405/12, 307/68; A61P 5/04  
US CL : 514/461, 275, 255; 549/506; 544/331, 405

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 514/461, 275, 255; 549/506; 544/331, 405

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
STN

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	✓ MNDZHOYAN et al. Synthesis of cephalosporin R-sulfoxides and their bactericidal properties, Khim.-Farm. Zh., 1988, Vol. 22 No. 9, see pages 1091-1094, especially compounds IX on page 1092..	9 & 10
X	✓ US 3,907,700 A (GRIER) 23 September 1975 (23.9.75) see column 21, lines 1 and 2.	9 & 10
X	✓ MNDZHOYAN et al. Investigations in the field of semisynthetic cephalosporins. I. Synthesis and antibacterial activity of some 7-substituted 3-methyl-3-cephem-4-carboxylic acids, Khim.-Farm. Zh., 1986, Vol 20 No. 4, see pages 446-450.	9 & 10
X	✓ US 5,622,976 A (TAKASUGI et al.) 22 April 1997 (22.04.97) column 51, lines 3-8.	9 & 10
X	✓ US 5,780,393 A (NEWTON) 14 July 1998 (14.07.98), columns 9 & 10, Table I, Example 15.	9 & 10
X	Chem. abstr., Vol 57, No. 9, 29 October 1962 (Columbus, OH, USA), the abstract 11137c, MNDZHOYAN, et al., "Some 5- and 4,5-substituted furfuryl- and tetrahydrofurfuryldialkylamines as the prospective cholinomimetic agents" see line 26, PhCH <sub>2</sub> , H, Pr.	9 & 10
A	GOULET, M.T. Gonadotropin Releasing Hormone Antagonists. In: Ann. Reports Med. Chem., 1995, Vol. 30, Chapter 18, pages 169-178.	1-10

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

14 March 2000 (14.03.2000)

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703)305-3230

Date of mailing of the international search report

21 AUG 2000

Authorized officer

Mark Berch, Ph.D.

Telephone No. (703) 308-1235

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/18790

Continuation of Item 4 of the first sheet: Title is too lengthy and generic, PCT Rule 4.3 The New title is:

"FURANYL GONADOTROPIN-RELEASING HORMONE AGENTS"

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING** This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-8, and claims 9-10 (in part) drawn to furans.

Group II, claim(s) 9-10 (in part), drawn to pyrroles.

Group III, claim(s) 9-10 (in part), drawn to imidazoles.

Group IV, claim(s) 9-10 (in part), drawn to pyrrazoles.

Group V, claim(s) 9-10 (in part), drawn to thiophenes.

Group VI, claim(s) 9-10 (in part), drawn to rings with both nitrogen and oxygen.

Group VII, claim(s) 9-10 (in part), drawn to rings with both nitrogen and sulfur.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the five membered ring labeled "het" is the special technical feature seen distinctively in each group. Without this ring, the remaining fragments would be non-novel.

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line IPEA/ US

# PCT

## CHAPTER II

### DEMAND

under Article 31 of the Patent Cooperation Treaty:  
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only	
Identification of IPEA	Date of receipt of DEMAND
<b>Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION</b> Applicant's or agent's file reference 0121-0002PCT	
International application No. PCT/US99/18790	International filing date (day/month/year) 20-August-1999 ( 20-08-99 ) (Earliest) Priority date (day/month/year) 20-August-1998 ( 20-08-98 )
Title of invention Non-Peptide GnRH Agents, Methods and Intermediates for Their Preparation	
<b>Box No. II APPLICANT(S)</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) Agouron Pharmaceuticals, Inc. 10350 North Torrey Pines Road La Jolla, California 92037 United States of America	Telephone No.:  Facsimile No.:  Teleprinter No.:
State (that is, country) of nationality: US	State (that is, country) of residence: US
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) ANDERSON, Mark Brian 41 Las Cascades Orinda, California 94563 United States of America	
State (that is, country) of nationality: US	State (that is, country) of residence: US
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) VAZIR, Haresh N. 10528 Caminito Pollo San Diego, California 92126 United States of America	
State (that is, country) of nationality: US	State (that is, country) of residence: US
<input checked="" type="checkbox"/> Further applicants are indicated on a continuation sheet.	

Sheet No. 2.

International application No.

PCT/US99/18790

## Continuation of Box No. II APPLICANT(S)

*If none of the following sub-boxes is used, this sheet is not to be included in the demand.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

LUTHIN, David Robert  
1772 Shadow Mountain Drive  
Encinitas, California 92024  
United States of America

State (that is, country) of nationality:  
USState (that is, country) of residence:  
US

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

PADERES, Genevieve DeGuzman  
5183 Sea Mist Court  
San Diego, California 92121  
United States of America

State (that is, country) of nationality:  
USState (that is, country) of residence:  
US

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

PATHAK, Ved P.  
4140-157 Via Candidiz  
San Diego, California 92130  
United States of America

State (that is, country) of nationality:  
CanadaState (that is, country) of residence:  
US

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

CHRISTIE, Lance Christopher  
518 Mynah Place  
Vista, California 92083  
United States of America

State (that is, country) of nationality:  
USState (that is, country) of residence:  
US

Further applicants are indicated on another continuation sheet.

## Continuation of Box No. II APPLICANT(S)

*If none of the following sub-boxes is used, this sheet is not to be included in the demand.*

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

HONG, Yufeng  
11980 Ashley Place  
San Diego, California 92128  
United States of America

State *(that is, country)* of nationality:  
China

State *(that is, country)* of residence:  
US

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

TOMPKINS, Eileen Valenzuela  
10129 West Lilac Road  
Escondido, California 92026  
United States of America

State *(that is, country)* of nationality:  
US

State *(that is, country)* of residence:  
US

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

LI, Haitao  
9699 Palmilla Drive #3112  
San Diego, California 92122  
United States of America

State *(that is, country)* of nationality:  
China

State *(that is, country)* of residence:  
US

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

FAUST, James  
15684 Bernardo Center Drive #2010  
San Diego, California 92127  
United States of America

State *(that is, country)* of nationality:  
US

State *(that is, country)* of residence:  
US



Further applicants are indicated on another continuation sheet.



**Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**

The following person is ☒ agent ☐ common representative  
 and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.  
☐ is hereby appointed and any earlier appointment of (an) agent(s) /common representative is hereby revoked.  
☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official  
The address must include postal code and name of country.)*

WOODWARD, David W.  
 SHANKS & HERBERT  
 TransPotomac Plaza  
 1033 North Fairfax Street, Suite 306  
 Alexandria, Virginia 22314  
 United States of America

Telephone No.:  
703-683-3600

Facsimile No.:  
703-683-9875

Teleprinter No.:

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

**Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION****Statement concerning amendments:\***

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filed.

the description ☐ as originally filed  
☐ as amended under Article 34

the claims ☐ as originally filed  
☐ as amended under Article 19 (together with any accompanying statement)  
☐ as amended under Article 34

the drawings ☐ as originally filed  
☐ as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

\* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

**Language for the purposes of international preliminary examination: English**

- ☒ which is the language in which the international application was filed.  
☐ which is the language of a translation furnished for the purposes of international search.  
☐ which is the language of publication of the international application.  
☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

**Box No. V ELECTION OF STATES**

The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

**Box No. VI CHECK LIST**

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- |   |   |        |
|---|---|--------|
| 1. translation of international application                             | : | sheets |
| 2. amendments under Article 34  | : | sheets |
| 3. copy (or where required, translation) of amendments under Article 19 | : | sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | sheets |
| 5. letter   | : | sheets |
| 6. other ( <i>specify</i> )   | : | sheets |

For International Preliminary Examining Authority use only

received      not received

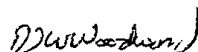
- |                          |                          |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

The demand is also accompanied by the item(s) marked below:

- |  |   |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet                             | 4. <input type="checkbox"/> statement explaining lack of signature                                  |
| 2. <input type="checkbox"/> separate signed power of attorney                            | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input checked="" type="checkbox"/> other ( <i>specify</i> ): check, postcard                    |

**Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE**

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

  
David W. Woodward  
Agent for Applicant

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:
2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):
3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply. ☐ The applicant has been informed accordingly.
4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.
5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

## PCT

## FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 40%;">International application No.</td> <td>PCT/US99/18790</td> </tr> <tr> <td>Applicant's or agent's file reference</td> <td>0121-0002PCT</td> </tr> </table>	International application No.	PCT/US99/18790	Applicant's or agent's file reference	0121-0002PCT	<div style="border: 1px solid black; padding: 5px;"> For International Preliminary Examining Authority use only </div> <div style="border: 1px solid black; padding: 5px; margin-top: 5px;"> Date stamp of the IPEA </div>
International application No.	PCT/US99/18790				
Applicant's or agent's file reference	0121-0002PCT				
Applicant <b>Agouron Pharmaceuticals, Inc., et al.</b>					
<b>Calculation of prescribed fees</b>  1. Preliminary examination fee ..... <span style="float: right;">490.00</span> <span style="border: 1px solid black; padding: 0 5px;">P</span>  2. Handling fee <i>(Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.)</i> ..... <span style="float: right;">153.00</span> <span style="border: 1px solid black; padding: 0 5px;">H</span>  3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box ..... <span style="float: right; border: 1px solid black; padding: 2px 10px;">643.00</span> <div style="text-align: right; border: 1px solid black; padding: 2px 10px; width: 150px; margin: 0 auto;">TOTAL</div>					
<b>Mode of Payment</b>  <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <input type="checkbox"/> authorization to charge deposit account with the IPEA (see below) </div> <div style="width: 45%;"> <input type="checkbox"/> cash </div> </div> <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <input checked="" type="checkbox"/> cheque </div> <div style="width: 45%;"> <input type="checkbox"/> revenue stamps </div> </div> <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <input type="checkbox"/> postal money order </div> <div style="width: 45%;"> <input type="checkbox"/> coupons </div> </div> <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <input type="checkbox"/> bank draft </div> <div style="width: 45%;"> <input type="checkbox"/> other (specify): </div> </div>					
<b>Deposit Account Authorization</b> <i>(this mode of payment may not be available at all IPEAs)</i>  The IPEA/ <u>US</u> <input type="checkbox"/> is hereby authorized to charge the total fees indicated above to my deposit account.  <input checked="" type="checkbox"/> <i>(this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit)</i> is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.					
<div style="display: flex; justify-content: space-between; align-items: flex-end;"> <div style="width: 30%;"> 50-0622  Deposit Account Number </div> <div style="width: 30%;"> <u>March 20 2000</u>  Date (day/month/year) </div> <div style="width: 30%;"> <u>NW Woodson</u>  Signature </div> </div>					

## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION CONCERNING  
SUBMISSION OR TRANSMITTAL  
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

HERBERT, Toni-Junell  
Shanks & Herbert  
TransPotomac Plaza  
Suite 306  
1033 N. Fairfax Street  
Alexandria, VA 22314  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 22 March 2000 (22.03.00)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference 0121-0002PCT	
International application No. PCT/US99/18790	
International publication date (day/month/year) Not yet published	
International filing date (day/month/year) 20 August 1999 (20.08.99)	Priority date (day/month/year) 20 August 1998 (20.08.98)
Applicant AGOURON PHARMACEUTICALS, INC. et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
3. An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT-receiving Office	Date of receipt of priority document
20 Augu 1998 (20.08.98)	60/097,520	US	20 Marc 2000 (20.03.00)

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MAR 30 2000

BY

Authorized officer

R. Chirém

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Telephone No. (41-22) 338.83.38

Form PCT/IB/304 (July 1998)

003181374

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 29 September 2000 (29.09.00)	
International application No. PCT/US99/18790	Applicant's or agent's file reference 0121-0002PCT
International filing date (day/month/year) 20 August 1999 (20.08.99)	Priority date (day/month/year) 20 August 1998 (20.08.98)
Applicant ANDERSON, Mark, Brian et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

20 March 2000 (20.03.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer H. Zhou Telephone No.: (41-22) 338.83.38
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**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> <b>A61K 31/34, 31/505, 31/50, C07D 405/12, 307/68, A61P 5/04</b>	<b>A3</b>	<b>(11) International Publication Number:</b> <b>WO 00/20358</b> <b>(43) International Publication Date:</b> 13 April 2000 (13.04.00)
<b>(21) International Application Number:</b> PCT/US99/18790 <b>(22) International Filing Date:</b> 20 August 1999 (20.08.99)  <b>(30) Priority Data:</b> 60/097,520 20 August 1998 (20.08.98) US  <b>(71) Applicant (for all designated States except US):</b> AGOURON PHARMACEUTICALS, INC. [US/US]; 10350 North Torrey Pines Road, La Jolla, CA 92037 (US).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> ANDERSON, Mark, Brian [US/US]; 41 Las Cascadas, Orinda, CA 94563 (US). VAZIR, Haresh, N. [US/US]; 10528 Caminito Pollo, San Diego, CA 92126 (US). LUTHIN, David, Robert [US/US]; 1772 Shadow Mountain Drive, Encinitas, CA 92024 (US). PADERES, Genevieve, DeGuzman [US/US]; 5183 Sea Mist Court, San Diego, CA 92121 (US). PATHAK, Ved, P. [CA/US]; 4140-157 Via Candidiz, San Diego, CA 92130 (US). CHRISTIE, Lance, Christopher [US/US]; 518 Mynah Place, Vista, CA 92083 (US). HONG, Yufeng [CN/US]; 11980 Ashley Place, San Diego, CA 92128 (US). TOMPKINS, Eileen, Valenzuela [US/US]; 10129 West Lilac Road, Escondido, CA 92026 (US). LI, Haitao [CN/US]; 9699 Palmilla Drive #3112, San Diego, CA 92122		<b>(US).</b> FAUST, James [US/US]; 15684 Bernardo Center Drive #2010, San Diego, CA 92127 (US).  <b>(74) Agents:</b> HERBERT, Toni-Junell; Shanks & Herbert, TransPotomac Plaza, Suite 306, 1033 N. Fairfax Street, Alexandria, VA 22314 (US) et al.  <b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>  <b>(88) Date of publication of the international search report:</b> 16 November 2000 (16.11.00)
<b>(54) Title:</b> NON-PEPTIDE GnRH AGENTS, METHODS AND INTERMEDIATES FOR THEIR PREPARATION  <b>(57) Abstract</b>  Non-peptide GnRH agents capable of inhibiting the effect of gonadotropin-releasing hormone are described. Such compounds and their pharmaceutically acceptable salts, multimers, prodrugs, and active metabolites are suitable for treating mammalian reproductive disorders and steroid hormone-dependent tumors as well as for regulating fertility, where suppression of gonadotropin release is indicated. Methods for synthesizing the compounds and intermediates useful in their preparation are also described.		

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DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/18790

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/34, 31/505, 31/50; C07D 405/12, 307/68; A61P 5/04

US CL : 514/461, 275, 255; 549/506; 544/331, 405

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/461, 275, 255; 549/506; 544/331, 405

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
STN

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MNDZHOYAN et al. Synthesis of cephalosporin R-sulfoxides and their bactericidal properties, Khim.-Farm. Zh., 1988, Vol. 22 No. 9, see pages 1091-1094, especially compounds IX on page 1092..	9 & 10
X	US 3,907,700 A (GRIER) 23 September 1975 (23.9.75) see column 21, lines 1 and 2.	9 & 10
X	MNDZHOYAN et al. Investigations in the field of semisynthetic cephalosporins. I. Synthesis and antibacterial activity of some 7-substituted 3-methyl-3-cephem-4-carboxylic acids, Khim.-Farm. Zh., 1986, Vol 20 No. 4, see pages 446-450.	9 & 10
X	US 5,622,976 A (TAKASUGI et al.) 22 April 1997 (22.04.97) column 51, lines 3-8.	9 & 10
X	US 5,780,393 A (NEWTON) 14 July 1998 (14.07.98), columns 9 & 10, Table I, Example 15.	9 & 10
X	Chem. abstr., Vol 57, No. 9, 29 October 1962 (Columbus, OH, USA), the abstract 11137c, MNDZHOYAN, et al., "Some 5- and 4,5-substituted furfuryl- and tetrahydrofurfuryldialkylamines as the prospective cholinomimetic agents" see line 26, PhCH2, H, Pr.	9 & 10
A	GOULET, M.T. Gonadotropin Releasing Hormone Antagonists. In: Ann. Reports Med. Chem., 1995, Vol. 30, Chapter 18, pages 169-178.	1-10

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

14 March 2000 (14.03.2000)

Date of mailing of the international search report

21 AUG 2000

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

Mark Berch, Ph.D.

Telephone No. (703) 308-1235



# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/18790

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/18790

**Continuation of Item 4 of the first sheet:** Title is too lengthy and generic, PCT Rule 4.3 The New title is:

"FURANYL GONADOTROPIN-RELEASING HORMONE AGENTS"

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING** This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-8, and claims 9-10 (in part) drawn to furans.

Group II, claim(s) 9-10 (in part), drawn to pyrroles.

Group III, claim(s) 9-10 (in part), drawn to imidazoles.

Group IV, claim(s) 9-10 (in part), drawn to pyrrazoles.

Group V, claim(s) 9-10 (in part), drawn to thiophenes.

Group VI, claim(s) 9-10 (in part), drawn to rings with both nitrogen and oxygen.

Group VII, claim(s) 9-10 (in part), drawn to rings with both nitrogen and sulfur.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the five membered ring labeled "het" is the special technical feature seen distinctively in each group. Without this ring, the remaining fragments would be non-novel.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
13 April 2000 (13.04.2000)

PCT

(10) International Publication Number  
**WO 00/20358 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 31/34**,  
31/505, 31/50, C07D 405/12, 307/68, A61P 5/04

[US/US]; 15684 Bernardo Center Drive #2010, San Diego,  
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(21) International Application Number: **PCT/US99/18790**

(74) Agents: **HERBERT, Toni-Junell; Shanks & Herbert**,  
TransPotomac Plaza, Suite 306, 1033 N. Fairfax Street,  
Alexandria, VA 22314 et al. (US).

(22) International Filing Date: 20 August 1999 (20.08.1999)

(25) Filing Language: English

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ,  
BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE,  
ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,  
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,  
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,  
SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,  
VN, YU, ZA, ZW.

(26) Publication Language: English

(30) Priority Data:  
60/097,520 20 August 1998 (20.08.1998) US

(71) Applicant (*for all designated States except US*):  
**AGOURON PHARMACEUTICALS, INC.** [US/US];  
10350 North Torrey Pines Road, La Jolla, CA 92037 (US).

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT,  
BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,  
NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,  
GN, GW, ML, MR, NE, SN, TD, TG).

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(75) Inventors/Applicants (*for US only*): **ANDERSON**,  
Mark, Brian [US/US]; 41 Las Cascadas, Orinda, CA  
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David, Robert [US/US]; 1772 Shadown Mountain Drive,  
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Via Candidiz, San Diego, CA 92130 (US). **CHRISTIE**,  
Lance, Christopher [US/US]; 518 Mynah Place, Vista,  
CA 92083 (US). **HONG**, Yufeng [CN/US]; 11980 Ashley  
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CA 92026 (US). **LI**, Haitao [CN/US]; 9699 Palmilla  
Drive #3112, San Diego, CA 92122 (US). **FAUST**, James

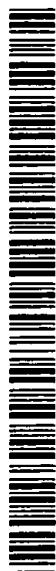
**Published:**

- With international search report.
- With amended claims and statement.

(88) Date of publication of the international search report:  
16 November 2000

Date of publication of the amended claims and statement:  
4 January 2001

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



**WO 00/20358 A3**

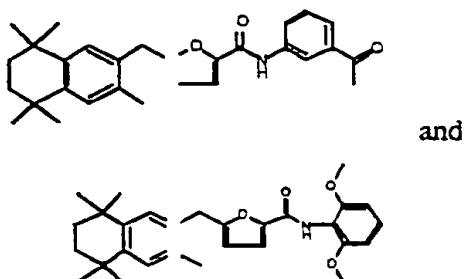
(54) Title: **NON-PEPTIDE GnRH AGENTS, METHODS AND INTERMEDIATES FOR THEIR PREPARATION**

(57) Abstract: Non-peptide GnRH agents capable of inhibiting the effect of gonadotropin-releasing hormone are described. Such compounds and their pharmaceutically acceptable salts, multimers, prodrugs, and active metabolites are suitable for treating mammalian reproductive disorders and steroid hormone-dependent tumors as well as for regulating fertility, where suppression of gonadotropin release is indicated. Methods for synthesizing the compounds and intermediates useful in their preparation are also described.

## AMENDED CLAIMS

[received by the International Bureau on 20 October 2000 (20.10.00);  
original claims 9 and 10 amended; new claims 11 and 12 added;  
remaining claims unchanged (6 pages)]

6. A compound having a formula selected from the group consisting of:

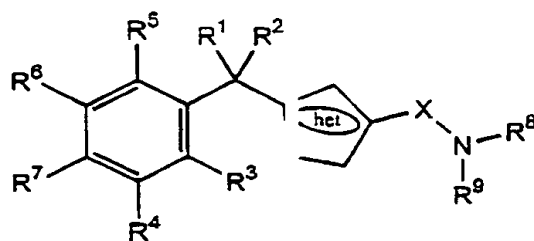


or a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof.

7. A pharmaceutical composition comprising: a therapeutically effective amount of a compound, pharmaceutically acceptable salt, multimer, prodrug, or active metabolite as defined in any of claims 1-6; and a pharmaceutically acceptable carrier or diluent.

8. A method for regulating the secretion of gonadotropins in mammals, comprising administering a therapeutically effective amount of a compound, pharmaceutically acceptable salt, multimer, prodrug, or active metabolite as defined in any of claims 1-6.

9. A compound of the Formula I:



I

where X is selected from C=O, C=S, S=O, and S(O)<sub>2</sub>;



is a 5-membered heterocyclic ring containing from 1 to 4 heteroatoms selected from N, O, and S, wherein the ring may be saturated, partially unsaturated, or fully unsaturated, and may be aromatic

$R^1$  and  $R^2$  are independently selected from H and lower alkyl;

$R^3$  is selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ , where R is selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, and heteroaryl, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

$R^4$  and  $R^5$  are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ , where R is as defined above; and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

$R^6$  and  $R^7$  are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ ; where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12; or  $R^6$  and  $R^7$  taken together with the atoms to which they are bonded form an optionally substituted 5- or 6-membered ring optionally having up to four heteroatoms selected from O, N, and S;

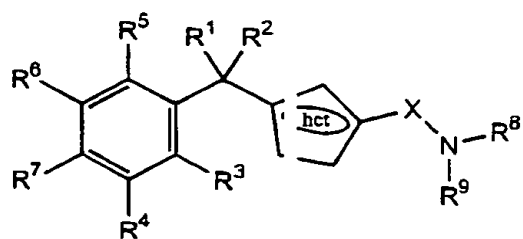
wherein at least one of  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ , and  $R^7$  is other than hydrogen;

$R^8$  is a lipophilic moiety selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ , where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 6 to 20; and

$R^9$  is selected from H and substituted and unsubstituted alkyl;

or a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof.

10. A compound of Formula I:



I

where X is selected from C=O, C=S, S=O, and S(O)<sub>2</sub>;



is a 5-membered heterocyclic ring containing from 1 to 4 heteroatoms selected from N, O, and S, wherein the ring may be saturated, partially unsaturated, or fully unsaturated, and may be aromatic;

R<sup>1</sup> and R<sup>2</sup> are independently selected from H and lower alkyl;

R<sup>3</sup> is selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH<sub>2</sub>OR, OR, and C(O)OR, where R is selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, and heteroaryl, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

R<sup>4</sup> and R<sup>5</sup> are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH<sub>2</sub>OR, OR, and C(O)OR, where R is as defined above; and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

R<sup>6</sup> and R<sup>7</sup> are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH<sub>2</sub>OR, OR, and C(O)OR; where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12; or R<sup>6</sup> and R<sup>7</sup> taken together with the atoms to which they are bonded form an optionally substituted 5- or 6-membered ring optionally having up to four heteroatoms selected from O, N, and S;

wherein at least one of R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> is other than hydrogen;

R<sup>8</sup> is a lipophilic moiety selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH<sub>2</sub>OR, OR, and C(O)OR,

where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 6 to 20; and

R<sup>9</sup> is selected from H and substituted and unsubstituted alkyl;

or R<sup>1</sup> or R<sup>2</sup> can be -OH or =O; and/or R<sup>8</sup> can also be hydrogen;

and/or R can be COR or hydrogen; and/or R<sup>8</sup> can have any desired number of carbon atoms;

and/or R<sup>8</sup> and R<sup>9</sup> can also form a ring; and/or any adjacent R groups, such as R<sup>5</sup> and R<sup>6</sup> or R<sup>3</sup> and R<sup>4</sup> can form a ring, such as those described for R<sup>6</sup> and R<sup>7</sup>;

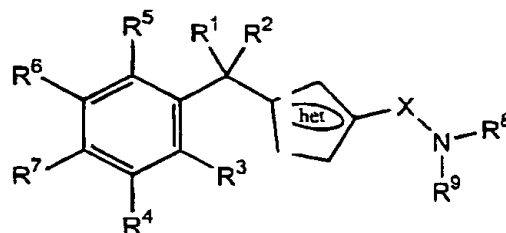
and/or R<sup>6</sup> can be COR; and/or the (het) group can be substituted or unsubstituted.

or R<sup>8</sup> and/or R<sup>9</sup> can be selected from heterocyclic groups or any compound that forms an amide bond with the nitrogen of Formula I;

or a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof.

11. A pharmaceutical composition comprising:

(a) therapeutically effective amount of a compound of the Formula I:



I

where X is selected from C=O, C=S, S=O, and S(O)<sub>2</sub>;



is a 5-membered heterocyclic ring containing from 1 to 4 heteroatoms selected from N, O, and S, wherein the ring may be saturated, partially unsaturated, or fully unsaturated, and may be aromatic

R<sup>1</sup> and R<sup>2</sup> are independently selected from H and lower alkyl;

R<sup>3</sup> is selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, CH<sub>2</sub>OR, OR, and C(O)OR, where R is selected from substituted and unsubstituted alkyl, alkenyl, alkynyl,

cycloalkyl, heterocycle, aryl, and heteroaryl, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

$R^4$  and  $R^5$  are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ , where R is as defined above; and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

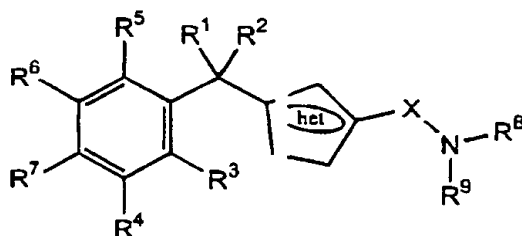
$R^6$  and  $R^7$  are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ ; where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12; or  $R^6$  and  $R^7$  taken together with the atoms to which they are bonded form an optionally substituted 5- or 6-membered ring optionally having up to four heteroatoms selected from O, N, and S;

$R^8$  is a lipophilic moiety selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ , where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 6 to 20;

$R^9$  is selected from H and substituted and unsubstituted alkyl; or a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof; and

(b) a pharmaceutically acceptable carrier or diluent.

12. A method for regulating the secretion of gonadotropins in mammals, comprising administering to a mammal in need of such regulation, a therapeutically effective amount of a compound of the formula I:



I

where X is selected from  $C=O$ ,  $C=S$ ,  $S=O$ , and  $S(O)_2$ ;





is a 5-membered heterocyclic ring containing from 1 to 4 heteroatoms selected from N, O, and S, wherein the ring may be saturated, partially unsaturated, or fully unsaturated, and may be aromatic;

$R^1$  and  $R^2$  are independently selected from H and lower alkyl;

$R^3$  is selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ , where R is selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, and heteroaryl, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

$R^4$  and  $R^5$  are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ , where R is as defined above; and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

$R^6$  and  $R^7$  are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ ; where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12; or  $R^6$  and  $R^7$  taken together with the atoms to which they are bonded form an optionally substituted 5- or 6-membered ring optically having up to four heteroatoms selected from O, N, and S;

$R^8$  is a lipophilic moiety selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl,  $CH_2OR$ ,  $OR$ , and  $C(O)OR$ , where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 6 to 20;

$R^9$  is selected from H and substituted and unsubstituted alkyl; or

a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof.

**STATEMENT UNDER ARTICLE 19**

Replacement sheets with amended claims 9 and 10, and new claims 11 and 12 (pages 436, 437, 438, 439, 440, 441 and 442) are provided herewith. Please note that claims 6-8 and the abstract remain unchanged. Claims 9 and 10 have been amended to clarify that at least one of R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> is other than hydrogen. This clarification more clearly distinguishes the claimed subject matter over the references cited in the International Search Report. Claims 9 and 10 have also been amended to clarify that they also cover pharmaceutically acceptable salts, polymers, prodrugs, and active metabolites of the compound. Claims 11 and 12 have been added. Claims 11 and 12 are parallel to claims 7 and 8, but define the compound as in original claim 9. It is submitted that the claims as amended herein do not extend beyond the disclosure of the international application as originally filed.

An Amendment under Article 19 must be filed within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. Applicants submit that this amendment is timely, being due on or before October 21, 2000 (the later of the two time limits), and that no fee is due. However, in the event any extensions of time or additional fees are required to prevent withdrawal of this application, then such extensions of time are hereby requested and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-0622.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

TECH CENTER 1600/2900

OCT 17 2001

RECEIVED

Applicant's or agent's file reference 0121-0002PCT		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/18790	International filing date (day/month/year) 20 August 1999 (20.08.1999)	Priority date (day/month/year) 20 August 1998 (20.08.1998)	
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/34, 31/505, 31/50; C07D 405/12, 307/68; A61P 5/04 and US Cl.: 514/461, 275, 255; 549/506; 544/331, 405			
Applicant AGOURON PHARMACEUTICALS, INC.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>455</u> sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input checked="" type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 20 March 2000 (20.03.2000)		Date of completion of this report 14 June 2001 (14.06.2001)	
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230		Authorized officer <i>Deepak Rao</i> Deepak Rao Telephone No. (703) 308-1235	

Form PCT/IPEA/409 (cover sheet)(July 1998)

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

International application No.

PCT/US99/18790

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☒ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

Group I, claim(s) 1-8, 11-12 and claims 9 & 10 in part, drawn to furans.

Group II, claim(s) claims 9 & 10, in part, drawn to pyrroles.

Group III, claim(s) claims 9 & 10, in part, drawn to imidazoles.

Group IV, claim(s) claims 9 & 10, in part, drawn to pyrrazoles.

Group V, claim(s) claims 9 & 10, in part, drawn to thiophenes.

Group VI, claim(s) claims 9 & 10, in part, drawn to rings with both nitrogen and oxygen.

Group VII, claim(s) claims 9 & 10, in part, drawn to rings with both nitrogen and sulfur.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. \_\_\_\_\_

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/18790

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

☐

the international application as originally filed.

☒

the description:

pages NONE as originally filedpages NONE, filed with the demandpages 1-433, filed with the letter of 28 September 2000 (28.09.2000)☒

the claims:

pages NONE, as originally filedpages 434 and 435, as amended (together with any statement) under Article 19pages NONE, filed with the demandpages 436-441, filed with the letter of 18 January 2001 (18.01.2001)☒

the drawings:

pages NONE, as originally filedpages NONE, filed with the demandpages 1-15, filed with the letter of 28 September 2000 (28.09.2000)☐

the sequence listing part of the description:

pages NONE, as originally filedpages NONE, filed with the demandpages NONE, filed with the letter of \_\_\_\_\_

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

☐

the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐

the language of publication of the international application (under Rule 48.3(b)).

☐

the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐

contained in the international application in printed form.

☐

filed together with the international application in computer readable form.

☐

furnished subsequently to this Authority in written form.

☐

furnished subsequently to this Authority in computer readable form.

☐

The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐

The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:☐the description, pages NONE☐the claims, Nos. NONE☐the drawings, sheets/fig NONE5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/18790

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. STATEMENT

Novelty (N)	Claims <u>1-12</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-12</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-12</u>	YES
	Claims <u>NONE</u>	NO

### 2. CITATIONS AND EXPLANATIONS (Rule 70.7)

Claims 1-12 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the species instantly claimed. The references of record teach unsubstituted phenyl ring or compounds wherein R3-R7 are hydrogen, whereas the instant compounds require that at least one of R3-R7 is other than hydrogen.

Claims 1-12 meet the criteria of industrial applicability set out in PCT Article 33(4), because the compounds are disclosed to be useful in inhibiting the effect of gonadotropin-releasing hormone.